

Clinical Evaluation of Low-Level Laser Treatment for Recurring Aphthous Stomatitis

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Abstract

Objective: The aim of the present study was to assess the effect of low-level laser on the control of pain and the repair of recurring aphthous stomatitis (RAS). **Background:** One of the most frequent pathologic conditions in the oral cavity is RAS. This multifactor immunologic inflammatory lesion causes patient discomfort, and treatment is controversial because of its unknown etiology. A number of treatment modalities have been proposed, but none is definitive. Low-level laser treatment (LLLT) has been used for lesions of an inflammatory nature, not as an inhibitor of the process, but for its modulating action and reparative effect on tissues. **Materials and Methods:** Twenty patients with RAS were divided into one group treated with a topical corticoid agent ($n = 5$) and another group treated with laser ($n = 15$). Group I received conventional treatment with triamcinolone acetonide 4 times per day. The patients in Group II received laser treatment with an InGaAlP diode laser with wavelength of 670 nm, 50 mW, 3 J/cm² per point in daily sessions (once per day) on consecutive days. Both treatments were applied until the disappearance of the lesions. All patients were evaluated on a daily basis, and the following clinical parameters were determined during each session: pain intensity before and after treatment and clinical measurement of lesion size. **Results:** The results revealed that 75% of the patients reported a reduction in pain in the same session after laser treatment, and total regression of the lesion occurred after 4 days. Total regression in the corticoid group was from 5 to 7 days. **Conclusion:** The use of LLLT under the conditions administered in the present study demonstrated analgesic and healing effects with regard to RAS.

Introduction

ONE OF THE MOST FREQUENT PATHOLOGIC conditions of the oral cavity is recurring aphthous stomatitis (RAS), also known as recurring aphthous ulcers.^{1–3} The prevalence of RAS in the world ranges from 5% to 60% of the population. In the United States, the highest incidence (60%) has been found to be among female nursing students and dental students (56%), whereas the lowest incidence has been found to be among hospitalized male patients. Approximately 1% of children in developed countries are affected by RAS, but it has been found that 40% of a selected group of children exhibit aphthous ulcers before the age of 5 years and that the frequency increases with age.⁴

Clinically, RAS is first seen as one or several round ulcerated lesions covered by a whitish pseudomembrane, with variable symptoms and a history of numerous recurrences. The etiology remains unknown, with autoimmune responses

and hypersensitivity the most widely discussed possibilities. Recent literature has demonstrated that no single factor or causal agent is responsible for RAS, but rather an interaction of cofactors of a systemic or local nature or both. RAS can therefore be considered a multifactor condition.^{1–3}

The diagnosis of RAS is based on a history of the condition and its clinical aspects. A number of treatment protocols have been suggested for RAS, but none has a curative effect. The basis of treatment is centered on the suppression/reduction of the local immune response, thereby diminishing discomfort and preventing secondary infection.^{1–3}

Low-level laser treatment (LLLT) has been widely used in pathologic processes, such as tissue repair and inflammatory conditions. Phototherapy basically accelerates the tissue-repair process in injuries and demonstrates antiinflammatory action. These effects may be related to the action of the laser, increasing cell metabolism, the regenerative potential of tissues, neovascularization, and the formation of scar tissue.^{5–10}

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Considering the high frequency of RAS and associated discomfort, as well as the antiinflammatory and reparative action of LLLT, the aim of the present study was to assess the clinical effect of the administration of low-level laser on RAS.

Materials and Methods

This study was approved by the Ethics Committee in Human Research, under number 131/2005. Twenty volunteer patients with minor RAS who sought the Dentistry Clinic of the Universidade Nove de Julho with a principal complaint of ulcers in the oral cavity were selected. After being informed of the risks and benefits of the procedures, all patients or those responsible signed terms of informed consent. The inclusion criteria were exclusively minor RAS; having received other treatments without satisfactory results; and not having undergone any other treatment in the previous 3 months. The exclusion criteria were systemic (endocrine-metabolic) disease; rheumatologic disease; hormone disorder; pregnancy; immunodeficiency; use of corticoid-based therapy; use of total or partial dentures; having restorations or teeth with sharp edges; and the use of orthodontic or other oral appliance. Patients who did not participate daily in the evaluations were excluded.

The patients were randomly selected, and among 40 patients who began treatment, only 20 completed the protocol. These were allocated into two groups: Group I, treatment with topical corticoid ($n=5$); and Group II, treatment with laser ($n=15$). All patients were submitted to a clinical examination (patient history + physical examination) on the first visit and responded to specific questions regarding the RAS condition, such as symptoms, number of lesions, average duration, frequency of episodes, possible triggering factors, and previous treatment for aphthous ulcers.

The patients in Group I received conventional treatment orientation for recurring aphthous lesions with the use of triamcinolone acetonide (Omcilon A; orabase) 4 times per day as long as the lesions were present. The patients returned to the clinic on consecutive days for evaluation until a complete regression of the lesions occurred.

The patients in Group II received laser irradiation with an InGaAlP diode laser (670-nm Laser Compacto KC 651; Kroman, São Bernardo do Campo, SP, Brazil). The power output and focal spot were fixed (50 mW and 1.9 cm, respectively). The energy density on the pen set was 3 J/cm^2 , and the exposure time was 1 min with 300 mJ of total energy dose. As the distance between the laser source and the surface of application is critical, the distance between the laser beam and mucosa was constant, with the pen touching the surface of the lesion.

Clinical evaluation was carried out in all sessions, recording the following clinical parameters: pain intensity before and after therapy: 0 (no pain), 1 (mild pain), 2 (moderate pain), and 3 (severe pain). The measurement of lesion size was determined every day, by using a millimeter ruler.

Statistical analysis of the data was performed by using tests for proportions for gender, predisposing factors for RAS, duration of time intervals between recurrences, symptoms, and lesions. A contingency table was used for the comparison between regression times in both groups, by using Fisher's Exact test. The level of significance was set at 5% of probability or the corresponding p value.

Results

Among the 20 patients evaluated, 60% ($n=12$) were female, and 40% ($n=8$) were male, aged between 1 and 70 years, with no significant difference between genders ($p=0.3428$). Ninety percent were nonsmokers. Sixty percent reported a family history of RAS. The main triggering factor for 57% of the patients ($n=12$) was stress, which differed significantly from the other factors reported, such as trauma (14.28%), foods (14.28%), menstruation (9.52%), and gastrointestinal disorders (4.76%). The main aspects of patients' data descriptions are listed in Table 1.

The recurrence interval for 60% of the patients ranged from 30 to 90 days (Table 2), which was significantly different from that of the remaining patients. Average duration of an episode ranged from 1 to 7 days for 69.23% of the patients.

The majority of the patients ($n=17$; $p<0.0001$) reported severe symptoms at the first evaluation. The site of the greatest incidence in 60% of cases was the labial mucosa (57.14%; $p<0.0001$).

Table 3 displays the duration of RAS according to treatment. The results revealed no significant difference in RAS regression time between the patients treated with corticoid agent and those treated with laser ($p=0.4345$).

Although no statistically significant difference was noted between groups, 86.60% of the patients having undergone laser treatment reported a reduction in pain in the same session ($p=0.0006$). Furthermore, in 40% of the cases, regression occurred an average of 4 days from the beginning of therapy.

Discussion

LLLT has been widely used in the health field, mainly for therapeutic purposes or for biostimulation because of its

TABLE 1. PATIENTS DEMOGRAPHICS, HABITS AND SPECIFIC HISTORY OF RAS CONDITION DATA

Patient	Age (yr)	Gender	Smoking	Triggering factor	Family history
1	23	Male	No	Stress	No
2	22	Female	No	Trauma	No
3	23	Male	No	No	No
4	28	Female	Yes	Stress	Yes
5	21	Female	No	Gastrointestinal disorders	Yes
6	23	Female	No	Stress	Yes
7	24	Female	No	Stress	Yes
8	30	Male	No	Stress	Yes
9	24	Male	No	Stress	Yes
10	23	Male	No	Food	No
11	26	Female	Yes	No	No
12	21	Female	No	Trauma	No
13	24	Male	No	Stress	Yes
14	21	Male	No	Food	No
15	4	Female	No	Food	No
16	19	Female	No	trauma, stress and menstruation	Yes
17	1	Female	No	Stress and menstruation	Yes
18	24	Male	No	Stress	Yes
19	70	Female	No	Stress	Yes
20	22	Female	No	Stress	Yes

TABLE 2. DISTRIBUTION OF TIME INTERVALS BETWEEN RAS EPISODES

Recurrence interval	No.	%
7-21 days	3	15.0
30-90 days	12	60.0
More than 90 days	2	10.0
Rarely	3	15.0
Total	20	100.0

$\chi^2 = 17.6; p = 0.0001.$

characteristics of low-level energy and wavelengths capable of penetrating tissues. A large number of studies have demonstrated the antiinflammatory capacity of this type of laser light as well as its action in the reduction of pain and stimulus for tissue repair.^{6,7,10-16}

The biostimulation by LLLT is dependent on laser-irradiation parameters such as wavelength, laser-output power, and energy density.⁵⁻⁸ In our study, we used an InGaAlP diode laser with 670 nm, 50 mW, and 3J/cm², parameters that have been used on oral mucositis with significant control of this inflammatory condition.¹⁶

The results of the present study showed that LLLT assists in the treatment of RAS, especially controlling pain when compared with treatment with a topical corticosteroid. The patients treated with LLLT exhibited a pain reduction since the first day, whereas the patient using a corticoid maintained the pain during all the treatment. Other studies evaluated the effect of laser treatment in RAS. However, most of them used CO₂ ablative laser¹⁷ and Nd:YAG.¹⁷⁻²¹ Sharon-Bulle *et al.*¹⁷ observed that carbon dioxide (CO₂) laser treatment with low energy levels (1-1.5 W) was effective in relieving pain due to large lesions in the oral cavity, thereby allowing continuation of radiotherapy to the critical therapeutic dose. Colvard and Kuo²³ used CO₂ laser in an ablative manner to treat oral aphthous ulcers. The procedure needed anesthesia, and in 88% of the cases, the ulcers were completely pain free after anesthetic resolution. Parkins *et al.*¹⁹ followed up 22 patients with both aphthous and herpetic lesions for 1 year after Nd:YAG laser treatment and described immediate relief of pain, faster healing, and less severe or no recurrence within 6 months. According to these authors, the laser treatment of RAS is more than a promising treatment.

The antiinflammatory and analgesic action of LLLT has been reported and also believed to be due to the fact that

low-level lasers lead to a reduction in the production of prostaglandin (PGE₂) or had effects on lymphocyte metabolism, including the activation of suppressor T lymphocytes and the modulation of the secretion of histamine, kinins, and tumor necrosis factor, which is thought to lead to a reduction in the inflammatory response^{5,24-26} and a consequent reduction in pain phenomena.

Another mechanism described for the action of laser on pain symptoms is the modulation of nociceptors through a change in the conduction of nerve impulses regarding pain and the release of endorphins and enkephalins after low-level laser therapy.²⁷

The comparison of RAS healing between the two treatments modalities used in this study showed that lesions disappeared several days earlier in the laser-treated group. Clinical and laboratory evidence has accumulated on a continuous basis, lending support to the use of low-level laser to promote wound repair as well as to reduce pain and inflammation.⁵⁻⁹ In wound repair, LLLT has been reported to accelerate tissue repair by stimulating the growth of mesenchymal, epithelial, and endothelial cells.

At present, no unifying theories on the pathogenesis of RAS exist. The immune mechanisms appear to play an essential role and probably involve a cell-mediated immune-response mechanism, with generation of T cells and tumor necrosis factor alpha (TNF- α) by these other leucocytes (macrophages and mast cells).²⁸ Studies have shown that RAS can be prevented by treatments that involve the synthesis of endogenous TNF- α , such as thalidomide and pentoxifylline.²⁸ The laser could affect the inflammatory process, causing a diminution of some cytokine levels, such as interleukin 1 β (IL-1 β), TNF- α , and interferon- γ (IFN)²⁹; however, their effects on RAS lesions were not established.

The administration of LLLT, which is widely used in inflammatory processes, not as an inhibitor of the process, but because of its modulating action, was of considerable value with regard to the aphthous ulcers evaluated in the present study. The results of the present study corroborate the theory that LLLT promotes pain control and assists in wound repair. Certainly, our study had some limitations. We believe that these findings are relevant and encourage the use of LLLT as a therapeutic tool in cases of RAS. However, further studies with different parameters (energy density, power, etc.) should be carried out to establish an ideal protocol for the use of LLLT in RAS.

Conclusion

We concluded that LLLT has an analgesic and wound-healing effect on recurring aphthous stomatitis.

Acknowledgments

We thank Richard Boike for his helpful comments and expertise with English grammar.

Author Disclosure Statement

No competing financial interests exist.

References

- Jurge, S., Kuffer, R., Scully, C., and Porter, S.R. (2006). Mucosal disease series, Number VI: recurrent aphthous stomatitis. *Oral Dis.* 12, 1-21.

TABLE 3. LESION REGRESSION TIME ACCORDING TO EXPERIMENTAL GROUP

Lesion regression time	Group I Corticoid agent		Group II Laser		p Value
	n	Percentage	n	Percentage	
5 days	2	40.0	10	66.8	0.5298
7 days	2	40.0	3	20.0	0.7656
8 days	0	0.0	1	6.6	1.0000
9 days	0	0.0	1	6.6	1.000
10 days	1	20.0	0	0.0	1.000
TOTAL	5	100.0	15	100.0	

$p = 0.4345$ with Fisher's Exact test.

2. Femiano, F., Lanza, A., Buonaiuto, C., et al. (2007). Guidelines for diagnosis and management of aphthous stomatitis. *Pediatr. Infect. Dis. J.* 26, 728–732.
3. Scully, C., and Porter, S. (2008). Oral mucosal disease: recurrent aphthous stomatitis. *Br. J. Oral Maxillofac. Surg.* 46, 198–206.
4. Scully, C., and Porter, S. (1989). Recurrent aphthous stomatitis: current concepts of etiology, pathogenesis and management. *J. Oral Pathol. Med.* 18, 21–27.
5. Almeida-Lopes, L., Rigau, J., Zangaro, R.A., Guidugli-Neto, J., and Jaeger, M.M. (2001). Comparison of the low level laser therapy effects on cultured human gingival fibroblasts proliferation using different irradiance and same fluence. *Lasers Surg. Med.* 29, 179–184.
6. Pereira, A.N., Eduardo, C. de P., Matson, E., and Marques, M.M. (2002). Effect of low-power laser irradiation on cell growth and procollagen synthesis of cultured fibroblasts. *Lasers Med. Sci.* 31, 263–267.
7. Marques, M.M., Pereira, A.N., Fujihara, N.A., Nogueira, F.N., and Eduardo, C.P. (2004). Effect of low-power laser irradiation on protein synthesis and ultrastructure of human gingival fibroblasts. *Lasers Surg. Med.* 34, 260–265.
8. Mester, E., Mester, A.F., and Mester, A. (1985). The biomedical effects of laser application. *Lasers Surg. Med.* 5, 31–39.
9. Longo, L., Evangelista, S., Tinacci, G., and Sesti, A.G. (1987). Effect of diodes-laser silver arsenide–aluminium (Ga–Al–As) 904nm on healing of experimental wounds. *Lasers Surg. Med.* 7, 444–447.
10. Kreisler, M., Christoffers, A.B., Al-Haj, H., Willershausen, B., and d’Hoedt, B. (2002). Low level 809-nm diode laser-induced in vitro stimulation of the proliferation of human gingival fibroblasts. *Lasers Surg. Med.* 30, 365–369.
11. Eduardo, F.P., Mehnert, D.U., Monezi, T.A., et al. (2007). Cultured epithelial cells response to phototherapy with low intensity laser. *Lasers Surg. Med.* 39, 365–372.
12. Dyson, M., and Yung, S.R. (1986). Effects of laser therapy on wound healing contraction and cellularity in mice. *Lasers Med. Sci.* 1, 125.
13. Kawakami, T., Ibaraki, I., Haraguchi, K., et al. (1989). The effectiveness of GaAlAs semiconductor laser treatment do decrease pain after irradiation. *Higashi Nippon Shigaku Zasshi* 8, 57–10.
14. Kudo, H.C., Inomata, K., Okajima, K., Moteji, M., and Oshiro, T. (1998). Low level laser therapy pain attenuation mechanisms I. *Laser Ther.* 1, 3–8.
15. Pinheiro, A.L., Cavalcanti, E.T., Pinheiro, T.I., Alves, M.J., and Manzi, C.T. (1997). Low-level laser therapy in the management of disorders of the maxillofacial region. *J. Clin. Laser Med. Surg.* 15, 181–183.
16. Schubert, M.M., Eduardo, F.P., Guthrie, K.A., et al. (2007). A phase III randomized double-blind placebo-controlled clinical trial to determine the efficacy of low level laser therapy for the prevention of oral mucositis in patients undergoing hematopoietic cell transplantation. *Support Care Cancer* 15, 1145–1154.
17. Sharon-Buller, A., and Sela, M. (2004). CO₂-laser treatment of ulcerative lesions. *Oral Surg. Oral Med. Oral Pathol. Oral Radiol. Endod.* 97, 332–334.
18. Convissar, R.A., and Massoumi-Sourey, M. (1992). Recurrent aphthous ulcers: etiology and laser ablation. *Gen. Dent.* 40, 512–515.
19. Parkins, F. (2000). Lasers in pediatric and adolescent dentistry. *Dent. Clin. North Am.* 44, 821–830.
20. Tezel, A., Kara, C., Balkaya, V., and Orbak, R. (2009). An evaluation of different treatments for recurrent aphthous stomatitis and patient perceptions: Nd:YAG laser versus medication. *Photomed. Laser Surg.* 27, 101–106.
21. Zand, N., Ataie-Fashtami, L., Djavid, G.E., et al. (2009). Relieving pain in minor aphthous stomatitis by a single session of non-thermal carbon dioxide laser irradiation. *Lasers Med. Sci.* 24, 515–520.
22. Convissar, R.A. (1992). Aphthous ulcers and lasers. *Oral Surg. Oral Med. Oral Pathol. Oral Radiol. Endod.* 82, 118.
23. Colvard, M., and Kuo, P. (1991). Managing aphthous ulcers: laser treatment applied. *J. Am. Dent. Assoc.* 122, 51–53.
24. Bortone, F., Santos, H.A., Albertini, R., Pesquero, J.B., Costa, M.S., and Silva, J.A., Jr. (2008). Low level laser therapy modulates kinin receptors mRNA expression in the sub-plantar muscle of rat paw subjected to carrageenan-induced inflammation. *Int. Immunopharmacol.* 8, 206–210.
25. Mafra, de Lima F., Costa, M.S., Albertini, R., Silva, J.A., Jr., and Aimbire, F. (2009). Low level laser therapy (LLLT): attenuation of cholinergic hyperreactivity, beta(2)-adrenergic hyporesponsiveness and TNF-alpha mRNA expression in rat bronchi segments in *E. coli* lipopolysaccharide-induced airway inflammation by a NF-kappaB dependent mechanism. *Lasers Surg. Med.* 41, 68–74.
26. Enwemeka, C., Parker, J.C., Dowdy, D.S., Harkness, E.E., Sanford, L.E., and Woodruff, L.D. (2004). The efficacy of low power lasers in tissue repair and pain control: a meta-analysis study. *Photomed. Laser Surg.* 22, 323–329.
27. Simunovic, Z., Ivankovich, A.D., and Depolo, A. (2000). Wound healing of animal and human body sport and traffic accident injuries using low-level laser therapy treatment: a randomized clinical study of seventy-four patients with control group. *J. Clin. Laser Med. Surg.* 18, 67–73.
28. Natah, S.S., Häyrynen-Immonen, R., Hietanen, J., Malmström, M., and Kontinen, Y.T. (2000). Immunolocalization of tumor necrosis factor-alpha expressing cells in recurrent aphthous ulcer lesions (RAU). *J. Oral Pathol. Med.* 29, 19–25.
29. Safavi, S.M., Kazemi, B., Esmaeili, M., Fallah, A., Modarresi, A., and Mir, M. (2008). Effects of low-level He-Ne laser irradiation on the gene expression of IL-1beta, TNF-alpha, IFN-gamma, TGF-beta, bFGF, and PDGF in rat’s gingiva. *Lasers Med. Sci.* 23, 331–335.

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