Low-level laser therapy (LLLT) in the treatment of recurrent aphthous stomatitis (RAS) – a promising treatment option: A report of two cases

Terapia laserem małej mocy w aftach nawrotowych – obiecująca opcja w leczeniu. Opis dwóch przypadków

Maria Olejnik[A–D], Zuzanna Ślebioda[B–D], Barbara Dorocka-Bobkowska[A,E,F]

Department of Gerodontology and Oral Pathology, Poznan University of Medical Sciences, Poland

A – research concept and design; B – collection and/or assembly of data; C – data analysis and interpretation;
D – writing the article; E – critical revision of the article; F – final approval of the article

Dental and Medical Problems, ISSN 1644-387X (print), ISSN 2300-9020 (online) *Dent Med Probl.* 2019;56(3):317–321

Address for correspondence
Maria Olejnik
E-mail: ipdmarole@gmail.com

Funding sources
None declared

Conflict of interest
None declared

Received on December 14, 2018
Reviewed on March 5, 2019
Accepted on April 18, 2019

Published online on September 30, 2019

Abstract

Recurrent aphthous stomatitis (RAS) is a chronic, ulcerative condition of the oral mucosa that affects 10–25% of the population. The etiopathogenesis of the disease is not fully understood, although a polygenic mode of inheritance and immunological dysregulation have been suggested in several studies. The contribution of numerous predisposing factors, such as a deficiency of iron, vitamin B12 or folic acid, trauma, emotional stress, endocrine disturbances, or allergy, have also been considered. So far, no causative treatment for RAS has been developed; instead, topical and systemic drugs are used to reduce pain and inflammation, and to lengthen the period of remission.

Low-level laser therapy (LLLT) is a non-invasive and atraumatic therapeutic method that involves the local application of a high-density, monochromatic, narrow-band light source. With the use of the appropriate power and wavelength, the therapy brings anti-inflammatory and analgesic results, and wound healing is promoted. Several reports on the beneficial effects of LLLT in RAS have been presented recently.

This report describes 2 cases of adult patients with RAS treated with LLLT to relieve pain and promote the healing of the ulcers. The clinical presentations with the signs and symptoms are discussed and illustrated, along with the treatment algorithms and outcomes.

Key words: oral mucosa, low-level laser therapy, aphthous stomatitis

Słowa kluczowe: błona śluzowa jamy ustnej, terapia laserem małej mocy, aftowe zapalenie jamy ustnej

Cite as
Olejnik M, Ślebioda Z, Dorocka-Bobkowska B. Low-level laser therapy 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

DOI
10.17219/dmp/108632

Introduction

Recurrent aphthous stomatitis (RAS; aphthae) is a common, painful, chronic inflammatory disease affecting up to 25% of the population, with a slightly higher prevalence in women and in groups of a higher socioeconomic status.[1,2] The etiopathogenesis of RAS remains unclear, but an abnormal immune interaction within the oral mucosal cells caused by the impaired activation of the immune system in genetically predisposed subjects has been considered to be an essential contributor in this process.[3–5] In aphthous lesions, the barrier function of the oral epithelium is destroyed. The exposure of danger-signal receptors, such as Toll-like receptors (TLRs), to pathogen- or microbe-associated (PAMP/MAMP) and damage-associated (DAMP) molecular patterns leads to an acute inflammatory reaction with cytokine production in the epithelial cells.[6] The possible modifiers of the immune system in RAS include various local and systemic factors, e.g., stress and anxiety, mineral and vitamin deficiencies, hematological disorders, viral and bacterial infections, food allergies, trauma, smoking, or even left- or right-handedness. Systemic diseases and medications have also been suggested as the potential triggers of RAS in several studies, although the results remain equivocal.[5,7,8]

Familial accumulation was observed in up to 40% of patients with RAS.[3,9] The genetic risk factors determining an individual's susceptibility to the disease include various DNA polymorphisms distributed in the human genome, especially those related to alterations in the metabolism of cytokines.[5,10] Recent research has suggested that dysregulation in the production of defensins might be involved in the development of several oral pathologies, including those with an autoimmune background.[6,11]

Aphthous lesions may be associated with systemic diseases, such as Behçet's disease, Crohn's disease, HIV infection, anemia, cyclic neutropenia, and celiac disease.[2,12] Recurrent aphthous lesions have been classified into 3 varieties: major (Sutton), minor (Mikulicz) and herpetiform ulcers. Minor aphthae present as yellowish, shallow, ovoid erosions surrounded by an erythematous halo, smaller than 5 mm in diameter. They heal within 10–14 days and are typically located on the non-keratinized oral mucosa (the floor of the mouth and the labial or buccal mucosa). Major aphthae appear as deep ulcers, larger than 10 mm in diameter, which heal within 6 weeks, sometimes leaving a scar. The lesions are painful and show a predilection for the soft palate, palatal fauces, lips, and tongue. Herpetiform aphthae are small (1–2 mm in diameter) and multiple (up to 100), occurring throughout the oral cavity and lasting for 7–10 days.[12,13]

The treatment of RAS is difficult and not always effective. The standard treatment regime includes the local application of steroids and non-steroidal anti-inflammatory drugs, together with agents which enhance epithelial regeneration. The therapy is mainly symptomatic and may lead to several side effects, including steroid-induced candidiasis. No effective causal treatment option is currently available.[1,2,12,13]

Low-level laser therapy (LLLT) involves the use of photons with non-thermal irradiance to alter biological activity. It is a non-invasive and atraumatic therapeutic method that involves the local application of a high-density, monochromatic, narrow-band light source. The main medical usage of LLLT is for pain and inflammation reduction, promoting the regeneration of different tissues and preventing damage to tissues. With the use of the appropriate power (from 5 to 200 mW) and wavelength (630–680 nm, 700–830 nm or 900 nm), the therapy brings anti-inflammatory and analgesic results, and wound healing is promoted.[14,15] The mechanism of action of LLLT may be very beneficial in the treatment of oral erosions and ulcers. There are few reports on accelerated healing in erosive mucocutaneous disorders and they are often presented as case series rather than large randomized clinical trials (RCTs). The effects on skin wound healing and periodontal inflammation management with laser biostimulation suggest that this treatment modality may also be useful for oral erosive conditions.[16,17]

This report describes 2 adult patients with RAS treated with LLLT to relieve pain and promote the healing of the ulcers. The clinical presentations with the signs and symptoms are discussed and illustrated, along with the treatment algorithms and outcomes.

Case reports

Case 1

A 25-year-old, generally healthy woman, reporting no detrimental habits was admitted to the Department of Gerodontology and Oral Pathology of Poznan University of Medical Sciences, Poland, with 2 painful ulcers on her tonsil and palatoglossal arch, which had developed 3 days earlier. Informed consent for examination was obtained from the patient as part of a routine protocol. According to the patient, the condition was recurrent, with flare-ups at 2–3-month intervals. The 1st episode appeared approx. 10 years earlier, and was exacerbated in the period 2009–2011, when she received orthodontic treatment with a fixed appliance. It was previously diagnosed as RAS by a general dentist. Usually, 1 or 2 major aphthae would appear simultaneously during a flare-up. The treatment of the previous lesions included a coating ointment composed of protein-free dialysate of calf blood and policresulen, which was not satisfactory for the patient. Upon admission, the patient suggested stress and tiredness as the cause for the lesions to recur.

On examination, 2 ulcers with an erythematous halo and fibrous coating, 2 cm in diameter, were revealed on the left tonsil and on the left palatoglossal arch (Fig. 1). Other regions of the oral mucosa were unaffected. The lymph nodes were normal. Due to the unfavorable location of the lesions and their large size, laser therapy was suggested. Low-level laser therapy was applied with a diode laser (DiodeLX, SMART M; Lasotronix, Piaseczno, Poland) set to a wavelength of 635 nm, a spot size of Ø 8 mm, a power of 100 mW, and an energy fluency of 4 J/cm^2 in continuous mode for 20 s per lesion (Fig. 2). It was administered 3 times – on the 1st, 3rd and 4th day of the therapy. A baseline complete blood count (CBC) test performed on the day of the 1st visit showed no abnormalities. After the 1st session, the ulcers were less painful and the process of healing was evident (Fig. 3). After 3 sessions, the lesions were painless and the patient reported faster healing than during the previous episodes of RAS (Fig. 4).

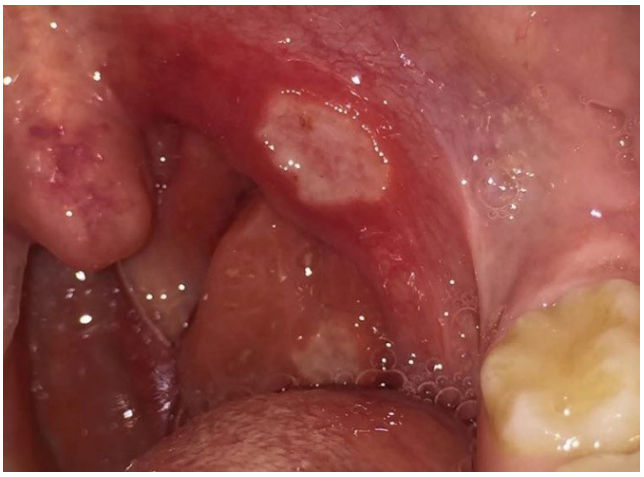

Fig. 1. Major aphthous ulcers on the tonsil and palatoglossal arch prior to treatment

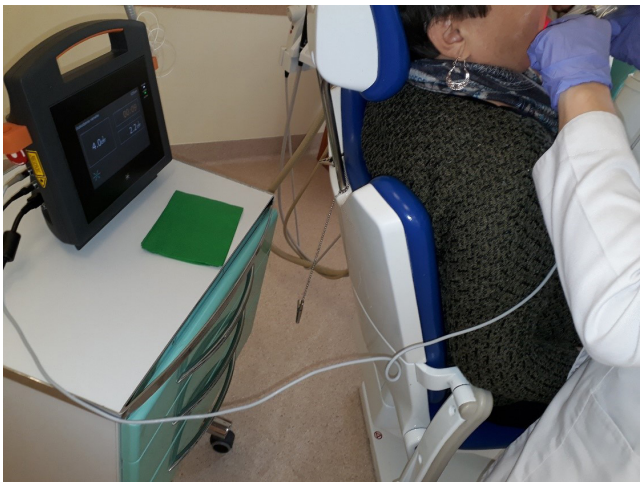

Fig. 2. SMART M diode laser with a wavelength of 635 nm and a spot size of Ø 8 mm

Fig. 3. Ulcers after the 1st session of low-level laser therapy (LLLT), showing the visible initiation of the healing process

Fig. 4. Ulcers after 3 sessions of low-level laser therapy (LLLT)

Case 2

An 81-year-old woman suffering from hypertension and type 2 diabetes (T2D) was admitted to the Department of Gerodontology and Oral Pathology of Poznan University of Medical Sciences, Poland, with a complaint of painful lesions in the oral cavity, which interfered with eating and speaking. Informed consent for examination was obtained from the patient as part of a routine protocol. The duration of the disease was 6 months with regular periods of remission and exacerbation. The patient had previously been treated by an otorhinolaryngologist and a general practitioner with topical choline salicylate, chlorhexidine mouth rinses and herbal extracts without satisfactory results. The CBC test results from the general outpatient clinic showed no abnormalities according to the patient.

Clinical examination revealed numerous minor aphthous erosions of the oral mucosa located on the buccal, labial, palatal, vestibular, gingival, tonsillar, and uvular surfaces (Fig. 5). Based on the anamnesis and the characteristic presentation of lesions, a diagnosis

of RAS was established. Low-level laser therapy was administered with a diode laser (DiodeLX, SMART M; Lasotronix) set to a wavelength of 635 nm, a spot size of Ø 8 mm, a power of 100 mW, and an energy fluency of 4 J/cm^2 in continuous mode for 20 s per lesion a total of 3 times – on the 1st, 2nd and 4th day of treatment.

Additionally, a topical steroid and a coating salve were prescribed and applied to the available surfaces.

After the 1st session, the patient claimed that her pain had lessened and after 3 sessions, a significant improvement in her clinical condition was observed (Fig. 6).

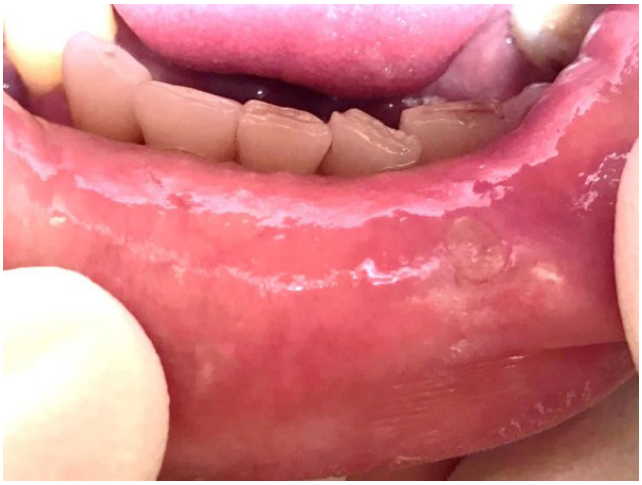

Fig. 5. Minor aphthous erosion on the labial surface prior to treatment

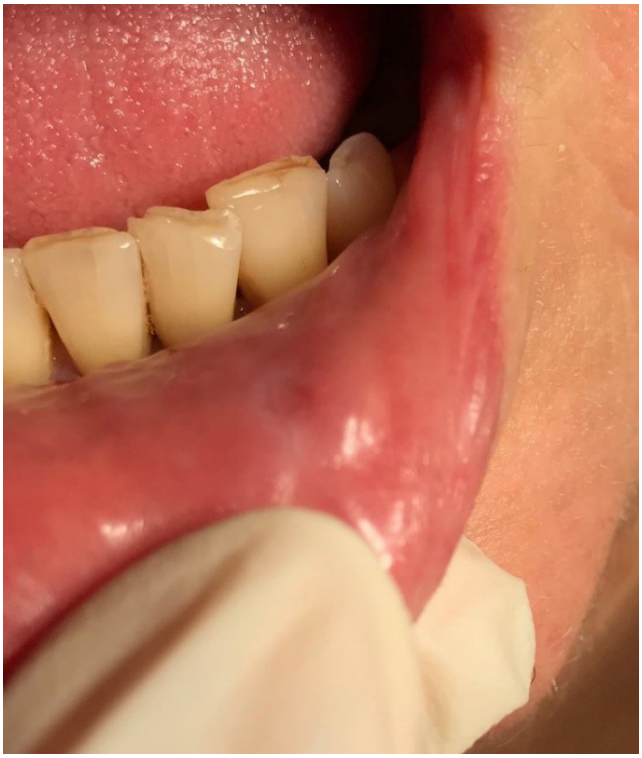

Fig. 6. Minor aphthous erosion on the labial surface after the 3rd session of low-level laser therapy (LLLT)

Discussion

Although several multi-center studies have been performed worldwide, the etiology of RAS remains elusive and only non-specific, symptomatic treatment is currently available. Pain management in RAS is a challenge in oral medical practice. A typical treatment algorithm begins with excluding systemic diseases and correcting any predisposing factors, such as nutritional deficiencies.[3,12,13] Treatment options include non-steroidal and steroidal agents, antibiotics to prevent secondary infections, analgesic drugs, and coating films. Topical corticosteroids, which are widely used in immune-mediated oral diseases, eliminate pain and shorten the healing time, although they may induce acute pseudomembrane candidiasis in non-immunocompetent patients, e.g., those who suffer from diabetes mellitus or are HIV-positive. Mouthwashes containing tetracycline or chlorhexidine may reduce ulcer duration, although they may also cause tooth discoloration and are contraindicated in children.[1,3,12] A topical coating salve prevents the irradiation of the lesions. Low-level laser therapy may be successfully administered as a non-invasive method to patients with large aphthous ulcers to accelerate the healing process.[18]

The cases described in this paper demonstrated the analgesic and healing-promoting effects of LLLT as the only therapy, and in combination with a topical steroid and a coating salve.

Several articles describing the effects of laser therapy in patients with RAS and lichen planus (LP) have been published in recent years. Diode, Nd:Yag and CO_2 lasers have been used in trials. The beneficial effects of LLLT with diode lasers which have been reported in RCTs on RAS include immediate pain reduction and a shorter healing time in comparison with the placebo groups.[19–22] Moreover, De Souza et al. reported faster regression of lesions when using LLLT than in patients treated with corticosteroids (4 days vs 5–7 days).[23] In 2 case series presented by Anand et al. and Gandhi Babu et al., pain relief and faster healing times were reported, compared to previous episodes, by all RAS subjects who underwent diode laser stimulation.[24,25] Recent studies performed by Lalabonova and Daskalov revealed a greater efficacy of LLLT as compared to conventional pharmacotherapy in reducing pain and the symptoms of inflammation, and in promoting healing and epithelialization.[26] Albrektson et al. showed the analgesic effect of LLLT after the 1st session, persisting for up to 3 days according to the visual analog scale (VAS). Patients also reported pain relief while eating, drinking and tooth brushing.[19] On the other hand, Jijin et al. presented similar results for both LLLT and amlexanox – a topical anti-inflammatory and anti-allergic drug.[27] Likewise, Kashmoola et al., who examined 47 RAS subjects in Iraq, did not observe significant differences in the healing time between the experimental groups and the controls.[28] Attempts to manage RAS with CO_2 lasers

in a non-contact, non-ablative manner, where the mucosa was protected from the heat produced by the laser with a thick layer of a transparent gel, also resulted in significant pain reduction with a sustained analgesic effect and an accelerated healing process.[16,17,20] The use of Nd:Yag laser stimulation in 2 RCTs resulted in pain relief and a faster healing time in the experimental group as compared to the controls,[29] and led to a significant analgesic effect in the experimental group.[30] The diversity of LLLT parameters used in many of the studies, including treatment dosage, wavelength, exposure time, or tissue type, prevents an unambiguous interpretation of the results.

Pain reduction and the acceleration of healing in the case of recurrent flare-ups are extremely relevant to the quality of life of patients with RAS. Further studies are required to define the efficacy of LLLT in the treatment of RAS in comparison with more traditional, anti-inflammatory treatment modalities.

Conclusions

Low-level laser therapy may be considered an effective and non-invasive method of reducing symptoms and promoting the healing of aphthous ulcers in patients with RAS without addressing the cause. There is, however, still an urgent need to develop an effective, causative treatment for RAS.

ORCID iDs

Maria Olejnik https://orcid.org/0000-0003-3474-2179
Zuzanna Ślebioda https://orcid.org/0000-0002-5482-3964
Barbara Dorocka-Bobkowska https://orcid.org/0000-0003-3659-7761

References

1. Belenguer-Guallar I, Jiménez-Soriano Y, Claramunt-Lozano A. Treatment of recurrent aphthous stomatitis. A literature review. *J Clin Exp Dent*. 2014;6(2):e168–e174.
2. Akintoye SO, Greenberg MS. Recurrent aphthous stomatitis. *Dent Clin North Am*. 2014;58(2):281–297.
3. Scully C, Gorsky M, Lozada-Nur F. The diagnosis and management of recurrent aphthous stomatitis: A consensus approach. *J Am Dent Assoc*. 2003;134(2):200–206.
4. Ślebioda Z, Szponar E, Kowalska A. Etiopathogenesis of recurrent aphthous stomatitis and the role of immunologic aspects: Literature review. *Arch Immunol Ther Exp (Warsz)*. 2014;62(3):205–215.
5. Ślebioda Z, Kowalska A, Rozmiarek M, Krawiecka E, Szponar E, Dorocka-Bobkowska B. The absence of an association between interleukin 1ß gene polymorphisms and recurrent aphthous stomatitis (RAS). *Arch Oral Biol*. 2017;84:45–49.
6. Al-Samadi A, Salem A, Ainola M, Hietanen J, Häyrinen-Immonen R, Konttinen YT. Increased beta 2 defensin in recurrent aphthous ulcer. *Oral Dis*. 2015;21(3):292–298.
7. Davies A, Gebremedhin S, Yee M, et al. Cationic porphyrin-mediated photodynamic inactivation of *Candida* biofilms and the effect of miconazole. *J Physiol Pharmacol*. 2016;67(5):777–783.
8. Dorocka-Bobkowska B, Düzgüneş N, Konopka K. AmBisome and Amphotericin B inhibit the initial adherence of *Candida albicans* to human epithelial cell lines, but do not cause yeast detachment. *Med Sci Monit*. 2009;15(9):BR262–BR269.
9. Ship JA, Chavez EM, Doerr PA, Henson BS, Sarmadi M. Recurrent aphthous stomatitis. *Quintessence Int*. 2000;31(2):95–112.
10. Guimarães AL, Correia-Silva Jde F, Sá AR, et al. Investigation of functional gene polymorphisms IL-1beta, IL-6, IL-10 and TNF-alpha in individuals with recurrent aphthous stomatitis. *Arch Oral Biol*. 2007;52(3):268–272.
11. Ślebioda Z, Szponar E, Kowalska A. Defensins and their role in the maintenance of the oral cavity homeostasis – a literature review. *Centr Eur J Immunol*. 2013;38(1):111–117.
12. Tarakji B, Gazal G, Al-Maweri SA, Azzeghaiby SN, Al Aizari NA. Guideline for the diagnosis and treatment of recurrent aphthous stomatitis for dental practitioners. *J Int Oral Health*. 2015;7(5):74–80.
13. Barrons RW. Treatment strategies for recurrent oral aphthous ulcers. *Am J Health Syst Pharm*. 2001;58(1):41–50.
14. Iwanicka-Grzegorek E, Puczyłowska-Rybaczyk M. Therapeutic and diagnostic application of laser in oral cavity diseases [in Polish]. *Nowa Stomat*. 2011;16(3):128–133.
15. Cotler HB, Chow RT, Hamblin MR, Carroll J. The use of low level laser therapy (LLLT) for musculoskeletal pain. *MOJ Orthop Rheumatol*. 2015;2(5):00068.
16. Owczarek B, Kiernicka M, Gałkowska E, Wysokińska-Miszczuk J. Influence of laser biostimulation on the healing of tissues in patients treated for chronic periodontitis [in Polish]. *Dent Med Probl*. 2004;41(1):45–49.
17. Hall G, Anneroth G, Schennings T, Zetterqvist L, Rydén H. Effect of low level energy laser irradiation on wound healing. An experimental study in rats. *Swed Dent J*. 1994;18(1–2):29–34.
18. Caputo BV, Noro-Filho GA, dos Santos CC, Okida Y, Giovani EM. Laser therapy of recurrent aphthous ulcer in patient with HIV infection. *Case Rep Med*. 2012;2012:695642.
19. Albrektson M, Hedström L, Bergh H. Recurrent aphthous stomatitis and pain management with low-level laser therapy: A randomized controlled trial. *Oral Surg Oral Med Oral Pathol Oral Radiol*. 2014;117(5):590–594.
20. Aggarwal H, Singh MP, Nahar P, Mathur H, Gv S. Efficacy of low-level laser therapy in treatment of recurrent aphthous ulcers – a sham-controlled, split mouth follow up study. *J Clin Diagn Res*. 2014;8(2):218–221.
21. Al Mulla F, Al Amari R, Zakaria D, Hemdan H. Diode laser treatment in aphthous ulcer for handicapped patients in Kuwait. *J Am Sci*. 2012;8(8):994–997.
22. Khademi H, Shirami AM, Nikegbal F. Evaluation of low level laser therapy in recurrent aphthous stomatitis. *Shiraz Univ Dent J*. 2009;10(2):160–162.
23. De Souza TO, Martins MA, Bussadori SK, et al. Clinical evaluation of low-level laser treatment for recurring aphthous stomatitis. *Photomed Laser Surg*. 2010;28(Suppl 2):S85–S88.
24. Anand V, Gulati M, Govila V, Anand B. Low level laser therapy in the treatment of aphthous ulcer. *Indian J Dent Res*. 2013;24(2):267–270.
25. Gandhi Babu DB, Chavva S, Waghray S, Jyothi Allam NS, Kondaiah M. Low level laser therapy to reduce recurrent oral ulcers in Behçet's disease. *Case Rep Dent*. 2016;2016:4283986.
26. Lalabonova H, Daskalov H. Clinical assessment of the therapeutic effect of low-level laser therapy on chronic recurrent aphthous stomatitis. *Biotechnol Biotechnol Equip*. 2014;28(5):929–933.
27. Jijin MJ, Rakaraddi M, Pai J, et al. Low-level laser therapy versus 5% amlexanox: A comparison of treatment effects in a cohort of patients with minor aphthous ulcers. *Oral Surg Oral Med Oral Pathol Oral Radiol*. 2016;121(3):269–273.
28. Kashmoola MA, Salman H, Al-Waez MM. Clinical effect of low level laser therapy on healing of recurrent aphthous ulcer and oral ulceration in Behcet's disease. *J Coll Dent*. 2005;17(2):36–40.
29. Arabaci T, Kara C, Ciçek Y. Relationship between periodontal parameters and Behçet's disease and evaluation of different treatments for oral recurrent aphthous stomatitis. *J Periodontal Res*. 2009;44(6):718–725.
30. Tezel A, Kara C, Balkaya V, Orbak R. An evaluation of different treatments for recurrent aphthous stomatitis and patient perceptions: Nd:YAG laser versus medication. *Photomed Laser Surg*. 2009;27(1):101–106.