Low-level laser therapy in the treatment of recurrent aphthous stomatitis and oral lichen planus: a literature review

Zuzanna Ślebioda, Barbara Dorocka-Bobkowska

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

Abstract

Recurrent aphthous stomatitis (RAS) and oral lichen planus (OLP) present inflammatory, recurrent diseases of the oral mucosa with not fully understood aetiology. Despite numerous attempts to discover an effective treatment for RAS and OLP, the current main treatment strategies are largely confined to the reduction of symptoms. Low-level laser therapy (LLLT) is of interest as a novel treatment modality. The aim of the paper was to discuss the mechanism of action and the biological effects of LLLT and to critically review and summarize recent clinical reports on the management of RAS and OLP. Most of the studies demonstrated the beneficial effect of LLLT in accelerating the healing process and pain reduction. However, the results should be interpreted with caution due to the limited number of studies available and empirical design using various irradiation parameters.

Key words: low-level laser therapy, recurrent aphthous stomatitis, lichen planus, oral pathology.

Introduction

The use of laser therapy, as a strategy to support the standard dental treatment regimes, has recently become very popular. In dental surgery and endodontic treatment, high-power lasers such as carbon-dioxide (CO₂), neodymium-doped yttrium aluminium garnet (Nd:YAG) or erbium-doped yttrium aluminium garnet (Er:YAG) have been commonly used. Meanwhile, semiconductor, low-power lasers are used in the physiotherapy of the oral mucosa and periodontium [1–5]. The history of clinical laser application dates back to the early 1960s, when the first low-level laser was invented by professor Ali Javan [6]. However, the popularization and the scientific acceptance of this treatment method has occurred only recently [7, 8].

The aim of the paper was to discuss the mechanism of action and biological effects of low-level laser therapy (LLLT) and to critically review and summarize recent clinical reports on the management of recurrent aphthous stomatitis (RAS) and oral lichen planus (OLP). In this review the studies published up to 2017 and obtained from Medline/PubMed online database were searched using the following key words: “laser”, “low-level laser therapy”, “recurrent aphthous stomatitis”, “oral lichen planus” and “lichen planus”. Language was limited to English. Randomized clinical trials, prospective studies and case reports were included in the analysis, while the fundamental experimental studies such as animal or cell studies, abstracts, reviews and editorials were excluded. Papers with insufficient information on phototherapy parameter settings or being duplicate studies were not discussed. The results of 21 full-text papers published in peer-reviewed journals are presented in the final summary.

Mechanism of action and biological effects of low-level laser therapy

Laser biostimulation of tissue is achieved by the application of a laser beam with a wave length from 630 to 1100 nm and with a power between 2 and 200 mW. The laser beam, which is monochromatic, coherent and parallel penetrates the tissue at depths up to 6 cm [2, 7, 9]. The penetration depth depends on the tissue vascularity and the energy dispersion by the erythrocytes. According to the first law of photobiology, molecular photoreceptors or chromophores must have absorption bands coinciding with the laser emissions for the phot-
The available results referring to skin wound healing are case series rather than large randomized clinical trials (RCTs). The mechanism of action of low-level laser therapy is multifaceted, although the mechanism of immunomodulation is not fully understood [12]. The laser irradiation results in the stimulation of blood circulation, revascularization, and the growth of nerve cells, fibroblasts and collagen fibres. It improves haemoglobin dissociation and increases the secretion of biological substances relevant in conducting nerve stimuli. LLLT does not result in tissue damage and overheating and it does not cause pain [7, 9, 13].

LLLT modulates the proliferation of fibroblasts, where the low power doses stimulate this process, while the high power doses result in its inhibition. The stimulation of the fibroblast proliferation occurs due to the increased production of basic fibroblast growth factor (bFGF). After the laser biostimulation, the transformation of the fibroblasts into myoblasts is accelerated, which is essential for the wound closure [14]. Moreover, it modifies the activity of macrophages by stimulating them to secrete several factors enhancing the proliferation of fibroblasts. LLLT increases the chemotactic activity of macrophages at the initial phase of healing [14, 15].

Laser therapy stimulates the differentiation of the epithelial cells while not disturbing the regularity of the process such as keratin synthesis. LLLT in low doses accelerates the collagen production which strengthens the scar. In post-operative wounds treated with LLLT the enhanced production of granulomatous tissue, earlier epithelization, efficient production of fibroblasts and active neovascularization have been observed. These processes result in decreased healing time and faster tissue regeneration [7, 14, 15].

The analgesic effect of LLLT results from the inhibition of several nociceptive stimuli, related to the temperature changes and chemical irritations. An increased pain threshold is also related to the stabilization of the cell membranes and regulation of the resting cell potential. LLLT limits the production of the proinflammatory mediators in the damaged nerve cells and it stimulates their maturation and post-traumatic regeneration [13–16].

The mechanism of action of low-level laser therapy may be very beneficial in the treatment of oral erosions and ulcers. Reports of healing acceleration in erosive mucocutaneous disorders are few and often presented as case series rather than large randomized clinical trials (RCTs). The available results referring to skin wound healing and periodontal inflammation management with laser biostimulation conclude that this treatment modality may also be useful for oral erosive conditions [3, 4, 17–19].

**Recurrent aphthous stomatitis and oral lichen planus**

Erosions and ulcers of the oral mucosa may be a manifestation of various pathologic conditions. Common oral mucosa diseases that occur with the presence of these lesions include RAS and OLP.

RAS is a chronic, ulcerative, inflammatory disease of the oral mucosa which affects between 5% and 20% of the general population [20, 21]. It manifests with recurrent, painful, round or oval erosions or ulcers surrounded with erythematous halo. The etiopathogenesis of this condition remains unclear, but it is probably multifactorial. In patients with RAS an inadequate immunologic response to certain trigger stimuli occurs. This includes mechanical irritation, stress, bacterial, viral or fungal antigens [22–24]. The inheritance of several gene polymorphisms, especially those related to the cytokine encoding genes, may predispose the development of the disease in one family members [20, 25]. Three clinical types of RAS can be distinguished: minor (Mikulicz’s, MiRAS), major (Sutton’s, MaRAS) and herpetiform (HeRAS). These types vary with lesion size and number during one flare-up, together with their localization and healing manner. The eruptions are painful and significantly decrease the patients’ quality of life [22, 26].

Lichen planus is a chronic inflammatory mucocutaneous disease which manifests with pink, flat, itchy papules on the skin in the area of wrists, forearms, dorsal surface of feet, calves, and lumbar region. Intraoral lesions present as white, non-removable striae composed of small papules, which is a primary eruption of OLP. The adjacent oral mucosa may be affected by the inflammation [12, 26]. While the exacerbations, the erosive or bullous forms may develop. The frequency of this condition is estimated to be 1% of the general population. It develops mostly in patients between 30 and 60 years of age. To date the etiopathogenesis of lichen planus has not been clearly understood and it involves both antigen-specific and non-specific mechanisms that include CD8+ cytotoxic T cells activity against keratinocytes, mast cell degranulation and activation of matrix metalloproteinase, which leads to the damage of the basal cell layer in the epithelium. Environmental factors including stress play a crucial role in the induction of the disease exacerbation [12, 27, 28].

The treatment of RAS and OLP is difficult and not always effective. The standard treatment regime includes the local application of steroids and non-steroidal anti-inflammatory agents, together with agents to enhance the epithelial regeneration. The therapy is mainly symptomatic and may lead to several side-effects, including steroid-induced candidiasis [29, 30]. No effective causative treatment option is currently available [12, 25, 28, 31].
**Low-level laser therapy in RAS and LP**

Several articles describing the effects of laser therapy in patients with RAS and LP have been published in recent years. Most were designed as RCTs, some as prospective studies or case series. Diode, Nd:YAG and CO₂ lasers have been utilized in the trials.

Table 1 depicts the most relevant international publications in this matter.

| Author          | Study population | Country | Study type | Laser used | Results                                                                 | Year |
|-----------------|------------------|---------|------------|------------|-------------------------------------------------------------------------|------|
| Aggarwal et al. | 30               | India   | RCT        | Diode      | Immediate pain relief and rapid reduction in the lesion size in the test group | 2014 |
| Albrektson et al.| 40               | Sweden  | RCT        | Diode      | Significant pain relief in the test group                               | 2014 |
| Al Mulla et al. | 147              | Kuwait  | RCT        | Diode      | Significant pain relief in the test group                               | 2012 |
| Anand et al.    | 2                | India   | Case series| Diode      | Pain reduction and shorter healing time compared to previous episodes    | 2013 |
| Arabaci et al.  | 28               | Turkey  | RCT        | Nd:YAG     | Pain relief and faster healing time in the test group                    | 2008 |
| Babu et al.     | 4                | India   | Case series| Diode      | Pain relief and faster healing time compared to previous episodes        | 2015 |
| De Souza et al. | 20               | Brazil  | RCT        | Diode      | Pain reduction and reduced healing time in the test group                | 2010 |
| Kashmoola et al.| 35               | Iraq    | RCT        | Diode      | No significant differences in healing time between study groups and controls | 2005 |
| Khademi et al.  | 24               | Iran    | RCT        | Diode      | Reduction in healing time, pain intensity and pain relief time in the test group | 2009 |
| Lalabonova et al.| 180             | Bulgaria| RCT        | Diode      | Significant pain relief and reduced healing time in the test group       | 2014 |
| Muñoz Sanchez et al. | 252         | Cuba    | RCT        | Diode      | Reduced healing time in the test group                                  | 2013 |
| Prasad et al.   | 25               | India   | RCT        | CO₂        | Immediate pain reduction and reduced healing time in the test group      | 2013 |
| Sattayut et al. | 14               | Thailand| RCT        | CO₂        | Significant pain relief in the test group; no difference in the lesion sizes | 2013 |
| Tezel et al.    | 20               | Turkey  | RCT        | Nd:YAG     | Significant pain relief in the test group                               | 2009 |
| Zand et al.     | 15               | Iran    | RCT        | CO₂        | Immediate, significant pain relief in the test group                     | 2009 |
| Cafaro et al.   | 30               | Italy   | Prospective| Diode      | Reduction in clinical symptoms defined by visual analogue scale (VAS)    | 2014 |
| El Shenawy et al.| 24              | Egypt   | RCT        | Diode      | Laser less effective than conventional steroids in pain reduction        | 2015 |
| Fornaini et al. | 19               | Italy   | Prospective| Diode      | Reduction of discomfort according to the NRS scale                      | 2012 |
| Kazancioglu and Ersen | 120         | Turkey  | RCT        | Diode      | Laser less effective than conventional steroids and ozone in pain reduction | 2015 |
| Mahdavi et al.  | 2                | Iran    | Case series| Diode      | Pain reduction, shift from ulcerative LP to reticular LP                 | 2013 |
| Misra et al.    | 1                | India   | Case report| Diode      | Total pain reduction                                                     | 2013 |
ous episodes, was reported by all the RAS subjects who underwent diode laser stimulation [38, 39]. Significant advantages of LLLT regarding pain reduction and healing time acceleration were achieved despite the different ranges of power applied, contact or non-contact use of the laser tip and a various period of irradiation. The suggested parameter settings ranged from 40 mW to 0.5 W of power output, wavelength between 670 and 810 nm, energy between 1.5 and 1.6 J, exposure time between 40 s and 3 min (with short intermissions) [32–39]. Contrary to the above-cited authors, Kashmoola et al., who examined 35 RAS subjects in Iraq, did not observe significant differences in healing time between study groups and controls [40]. The diode laser used in that study had an average diode power of 8 mW and wavelength of 904 nm. Laser irradiation with the energy of 1.5 J for 5 min was applied in the study subgroups on two following days. Considering the results of previously cited studies this observation is unexpected. Lack of any significant difference in the healing time between laser-treated and untreated RAS subjects suggest that the dose and other parameters of LLLT implementation influence the effectiveness of the therapy. It should be also emphasized that most of the cited studies were performed on a relatively low number of patients, therefore for more conclusive results a necessity to perform more extended observation in this field is evident.

Attempts to manage RAS with CO2 lasers in a non-contact, non-ablative manner, where the mucosa was protected from the heat produced by laser with a thick layer of transparent gel, also resulted in significant pain reduction with sustained analgesic effects and accelerated healing processes [41–43]. Zand et al. observed immediate reduction of pain directly after the laser irradiation [41]. Also Prasad and Pai who used CO2 laser with a reduced wattage compared to the previously described study (0.7 W, 5–8 s) reported immediate and significant pain reduction in RAS patients after a single session of laser irradiation. Moreover, the healing time was also significantly reduced in the study group compared to placebo [42]. Suggested mechanisms which explain the analgesic action of non-ablative CO2 laser include the direct effect on the exposed nerve endings present in the aphtous ulceration, suppression of inflammatory mediators or, less probably, the destruction of the nerve endings. The healing process is supported by the laser irradiation via various paths described in the section “Mechanism of action and biological effects of low-level laser therapy (LLLT)” above. It includes the stimulation of blood circulation, revascularization, and the growth of nerve cells, fibroblasts and collagen fibres. Meanwhile, no differences in the time of lesion size reduction between the tested groups were observed by Sattayut et al., who reported only the analgesic effect of LLLT. However, significant differences in the pain perception appeared not immediately (like in the previous studies) but after 3 days of irradiation with a defocused 10.6 micron CO2 laser in a continuous wave mode (2 W, 5 s) [43]. High density of energy used in this study (110.67 J/cm2) could explain the inhibitory effect of pain relief rather than stimulation of wound healing as in several in vitro studies it was demonstrated that while the low doses of low-intensity laser promoted the cellular proliferation, the doses over 16 J/cm2 inhibited the process. A contrary effect was observed in relation to the prostaglandin E2 production, which was stimulated at lower and inhibited at higher energy density [44, 45].

The use of Nd:YAG laser stimulation in the two RCTs also caused the pain relief and faster healing time in the test group compared to controls [46] and a significant analgesic effect in the study group [47]. Arabaci et al. who used the following irradiation parameters: power output: 2 W, energy: 100 mJ, frequency: 20 Hz, emission mode: pulsed, irradiation time: 2–3 min, and a contact mode of application, reported immediate and significantly higher pain reduction in the RAS group treated with laser compared to controls who received topical corticosteroids [46].

Malignant diseases and precancerous lesions are listed as contraindications for LLLT since it stimulates the growth of cells, therefore, according to some authors, the use of this treatment modality should be generally avoided in patients with OLP [9]. The stimulating effect of LLLT on various cell lines is dose-dependent and still not well understood. For example, in a Powell et al. in vitro study on selected cell lines, certain doses of laser increased the proliferation of human breast adenocarcinoma, however multiple exposures had either no effect or showed negative dose response relationships and generally no sign of malignant transformation of cells by laser phototherapy was detected in the study [48]. Although a number of studies suggest an increased risk of oral squamous cell carcinoma (OSCC) related to OLP, only a few researches demonstrated significant differences in comparison to a general population [49, 50]. This risk varies between 0% and 12.5% and this large heterogeneity of results is caused, among the others, by ambiguous diagnostic criteria or various follow-up periods used in different medical centres [50]. Based on the recent meta-analysis by Aghbari et al., only a small subset of OLP patients (1.1%) develop OSCC [51].

The described effects of LLLT in the treatment of OLP included the reduction of pain and discomfort and – in most cases the remission of exacerbated lesions [27, 52–54]. Soliman et al. observed marked clinical improvement in over 60% of examined patients with OLP after diode laser irradiation [53]. In their case report series, Mahdavi...
et al. observed a shift from ulcerative OLP to reticular OLP after LLLT [54]. However, in the two described RCTs the analgesic effect of diode laser therapy was less evident than in case of standard topical steroidal treatment [55, 56]. Moreover, Kazancioglu and Erisen found that it was also less effective than ozone therapy [55]. Most commonly used diode laser settings were as follows: output power of 300 mW, wavelength between 630 and 980 nm, the power density of 1 W/cm² and repeated mode of application [27, 54, 56]. As in case of RAS, the beneficial effects of LLLT in the treatment of OLP could be explained by dose-dependent lowering of prostaglandin E2 and interleukin 1β levels at the peripheral level, modification of metabolism and release of serotonin and acetylcholine at the central level, and by the reduction of oxidative stress [55, 56].

Although the benefits of using CO2 lasers in a non-contact, non-ablative manner for several erosive mucosal conditions, such as RAS, Behçet’s disease, pemphigus vulgaris or mucositis have been reported, not much is known on the effect of that treatment modality in OLP [7, 9]. Meanwhile, a traditional, high-power CO2 approach to treat recurrent, erosive OLP was suggested by Mücke et al. who observed a decreased risk of malignant transformation and reduced rate of recurrences in subjects who underwent CO2 laser vaporization compared to controls on topical, symptomatic treatment. The authors defined this treatment option as an independent significant factor reducing malignant transformation in OLP. In this study 9.4% out of 171 OLP subjects developed oral squamous cell carcinoma: 2 (2.9%) patients after continuous defocused CO2 laser treatment and 14 (13.6%) patients undergoing conservative treatment only [57]. It must be emphasized however that laser vaporization instead of biostimulation was studied in this research, therefore a potential effect of malignant cell growth stimulation was not observed here. The use of LLLT in erosive OLP as a potential premalignant condition remains controversial.

Conclusions

Low-level laser treatment has been used for lesions of an inflammatory nature, not as an inhibitor of the process, but as a modulating action and reparative effect on tissues. Based on the research presented, it seems that LLLT presents as a reasonable treatment modality both in RAS and OLP and could be incorporated into a standard treatment algorithm under these conditions. Based on the studies presented, the beneficial effects of LLLT were more evident in the case of RAS than in OLP, where in the two cited RCTs laser therapy was less effective than topical steroidal treatment. Pain reduction and acceleration of healing in the case of recurrent exacerbations are extremely relevant to the quality of life in patients with RAS and OLP. Further studies are required to define the efficacy of LLLT in the treatment of RAS and OLP in comparison to more traditional, anti-inflammatory treatment modalities that also include topical steroidal therapy. Since lasers were first introduced into dentistry it has become necessary to establish simultaneously most useful and least harmful irradiation parameters, including wavelength, energy density, continuous or pulsed mode, time of exposure and focal spot. A diversity of LLLT parameters used in the presented studies impede the unambiguous interpretation of the results.

It should be emphasized however that LLLT helps to reduce the symptoms of existing diseases without addressing the cause. Therefore, there is an urgent necessity to develop an effective, causative treatment for RAS and OLP.

Conflict of interest

The authors declare no conflict of interest.

References

1. Asnaashari M, Zadsirjan S. Application of laser in oral surgery. J Lasers Med Sci 2014; 5: 97-107.
2. Parker S. Low-level laser use in dentistry. Br Dent J 2007; 202: 131-8.
3. Ghadimi S, Chiniforush N, Bouraima SA, Jafari M. Clinical approach of laser application in different aspects of pediatric dentistry. 1 Lasers Med Sci 2012; 3: 84-90.
4. Owczarek B, Kiernicka M, Galkowska E, Wysokińska-Misczuk J. Wpływ biostymulacji laserowej na gojenie tnaków u pacjentów leczonych z powodu przewlekłego zapałenia przyębia. Dent Med Probl 2014; 41: 45-9.
5. Szyszkowska A, Hamwi R, Koliński P. Zabiegi fizjoterapeutyczne stosowane w leczeniu stomatologicznym. Implantoprotezyka 2011; 1-2: 42-3.
6. Javan A, Ballik EA, Bond WL. Frequency characteristics of a continuous-wave He-Ne optical maser. J Opt Soc Amer 1962: 52: 96.
7. Zand N. Non-thermal, non-ablative CO2 laser therapy (NACLIT): a new approach to relieve pain in some painful oral diseases. In: CO2 laser optimization and application. Dumitras DC (ed). InTech 2012: 387-414.
8. Hamblin MR. Introduction to experimental and clinical studies using low-level laser (light) therapy (LLT). Lasers Surg Med 2010; 42: 447-9.
9. Vučičević Boras V, Vidović Juras D, Andabak Rogulj A, et al. Applications of low level laser therapy. In: A Textbook of Advanced Oral and Maxillofacial Surgery, Motamedi MHK (ed). InTech 2013: 327-39.
10. Sutherland JC. Biological effects of polychromatic light. Photochem Photobiol 2002; 76: 164-70.
11. Calderhead RG. The photobiological basics behind light-emitting diode (LED) phototherapy. Laser Ther 2007; 16: 97-108.
12. Yang H, Wu Y, Ma H, et al. Possible alternative therapies for oral lichen planus cases refractory to steroid therapies. Oral Surg Oral Med Oral Pathol Oral Radiol 2016; 121: 496-509.
13. Basiirat M. The effects of the low power lasers in the healing of the oral ulcers. J Lasers Med Sci 2012; 3: 79-83.
14. Walsh JL. The current status of low level laser therapy in dentistry. Part 1. Soft Tissue applications. Aust Dent J 1997; 42: 247-54.
15. Iwanicka-Grzegorek E, Puczylowska-Rybczyk M. Terapeutyczne i diagnostyczne zastosowanie lasera w schorzeniach jamy ustnej. Nowa Stomatologia 2011; 3: 128-33.

16. Agha MT. Low-level laser therapy as a solution in a dental clinic: a review and case report. J Oral Laser Application 2007; 7: 65-73.

17. Takeda Y. Irradiation effect of low-energy laser on alveolar bone after tooth extraction. Experimental study in rats. Int J Oral Maxillofac Surg 1988; 17: 388-91.

18. Hall G, Anneroth G, Schennings T, et al. Effect of low level energy laser irradiation on wound healing. An experimental study in rats. Swed Dent J 1994; 18: 29-34.

19. Bisht D, Gupta SC, Misra V, et al. Effect of low intensity laser radiation on healing of open skin wounds in rats. Indian J Med Res 1994; 100: 43-6.

20. Vale FA, Moreira MS, de Almeida FC, Ramalho KM. Low-level laser therapy in the treatment of recurrent aphthous ulcers: a systematic review. Sci World J 2015; 2015: 150412.

21. Altenburg A, Abdel-Naser MB, Seeber H, et al. Practical aspects of management of recurrent aphthous stomatitis. J Eur Acad Dermatol Venereol 2007; 21: 1019-26.

22. Koybasi S, Parlak AH, Serin E, et al. Recurrent aphthous stomatitis: investigation of possible etiologic factors. Am J Otolaryngol 2006; 27: 229-32.

23. Ślebioda Z, Szponar E, Kowalska A. Etiopathogenesis of recurrent aphthous stomatitis and the role of immunologic aspects: literature review. Arch Immun Ther 2014; 62: 205-15.

24. Gebremedhin S, Dorocka-Bobkowska B, Przyliński M, et al. Miconazole activity against Candida biofilms developed on cultured discis. J Physiol Pharmacol 2014; 65: 593-600.

25. Belenguer-Guallar I, Jiménez-Soriano Y, Claramunt-Lozano M. Treatment of recurrent aphthous stomatitis. A literature review. J Clin Exp Dent 2014; 6: e168-74.

26. Gorouhi F, Davari F, Fazel N. Cutaneous and mucosal lichen planus: a comprehensive review of clinical subtypes, risk factors, diagnosis, and prognosis. Sci World J 2014; 2014: 742826.

27. Cafaro A, Arduino PG, Massolini G, et al. Clinical evaluation of the efficiency of low-level laser therapy for oral lichen planus: a prospective case series. Laser Med Sci 2014; 29: 185-90.

28. Pavlic V, Vujic-Aleksic V, Aoki A, Nezic L. Treatment of recurrent aphthous stomatitis by laser therapy: a systematic review of the literature. Vojnosanit Pregl 2015; 72: 722-8.

29. 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: 777-83.

30. Dorocka-Bobkowska B, Düzgünş 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: BR262-9.

31. Najeeb S, Khurshid Z, Zohaib S, et al. Management of recurrent aphthous ulcers using low-level lasers: a systematic review. Medicina 2016; 52: 263-8.

32. Aggarwal H, Singh MP, Nahar P, et al. 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: 218-21.

33. Albrektsson M, Hedström L, Bergh H. Recurrent aphthous stomatitis and pain management with low-laser therapy: a randomized, controlled trial. Oral Surg Oral Med Oral Pathol Oral Radiol 2014; 117: 590-4.

34. 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: 994-7.

35. Khadem H, Shirami AM, Nikegbal F. Evaluation of low level laser therapy in recurrent aphthous stomatitis. Shiraz Univ Dent J 2009; 10: 160-2.

36. 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: 929-33.

37. De Souza TOF, Martins MAT, Bussadori SK, et al. Clinical evaluation of low-level laser treatment for recurring aphthous stomatitis. Photomed Laser Surg 2010; 28: S85-8.

38. Anand V, Gulati M, Govila V, Anand B. Low level laser therapy in the treatment of aphthous ulcer. Indian J Dent Res 2013; 24: 26770.

39. Babu B, Uppada UK, Tarakji B, et al. Versatility of diode lasers in low-level laser therapy for the management of recurrent aphthous stomatitis. J Oropharyngol 2017; 4: 49-53.

40. KashmooLA AL, 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 Dentistry 2005; 17: 36-40.

41. Zand N, Ataie-Fashami L, Djavide G, et al. Relieving pain in minor aphthous stomatitis by a single session of non-thermal carbon dioxide laser irradiation. Lasers Med Sci 2009; 24: 515-20.

42. Prasad RS, Pai A. Assessment of immediate pain relief with laser treatment in recurrent aphthous stomatitis. Oral Surg Oral Med Oral Pathol Oral Radiol 2013; 116: 189-93.

43. Sattayut S, Trivibulwanich J, Pipithirunkarn N, Danvirutai N. A clinical efficacy of using CO2 laser irradiating to transparent gel on aphthous stomatitis patients. Laser Ther 2013; 22: 283-9.

44. Hawkins DH, Abrahamse H. The role of laser fluence in cell viability, proliferation, and membrane integrity of wounded human skin fibroblasts following helium-neon laser irradiation. Lasers Surg Med 2006; 38: 74-83.

45. Sattayut S, Hughes F, Bradley P. 820 mm gallium aluminium arsenide laser modulation of prostaglandin E2 production in interleukin 1 stimulated myoblasts. Laser Ther 1999; 11: 88-95.

46. 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 Periodontol Res 2009; 44: 718-25.

47. 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: 101-6.

48. Powell K, Low P, McDonnell PA, et al. The effect of laser irradiation on proliferation of human breast carcinoma, melanoma, and immunomammary epithelial cells. Photomed Laser Surg 2010; 28: 115-23.

49. Barnard NA, Scully C, Eveson JW, et al. Oral cancer development in patients with oral lichen planus. J Oral Pathol Med 1993; 22: 421-4.

50. Gandofo S, Richardi L, Carozzo M, et al. Risk of oral squamous cell carcinoma in 402 patients with oral lichen planus: a follow-up study in an Italian population. Oral Oncol 2004; 40: 77-83.

51. Aghbari SMH, Abushouk AI, Attia A, et al. Malignant transformation of oral lichen planus and oral lichenoid lesions:
a meta-analysis of 20095 patient data. Oral Oncol 2017; 68: 92-102.
52. Fornaini C. LLLT in the symptomatic treatment of oral lichen planus. Laser Ther 2012; 21: 51-3.
53. Soliman M, Kharbotly AE, Saafan A. Management of oral lichen planus using diode laser (980 nm). A clinical study. Egypt Dermatol Online J 2005; 1: 3-12.
54. Mahdavi O, Boostani N, Jajarm HH, et al. Use of low level laser therapy for oral lichen planus: report of two cases. J Dent Shiraz Univ Med Sci 2013; 14: 201-4.
55. Kazancioglu HO, Erisen M. Comparison of low-level laser therapy versus ozone therapy in the treatment of oral lichen planus. Ann Dermatol 2015; 27: 485-91.
56. El Shenawy HM, Eldin AM, Abdelmonem A. Clinical assessment of the efficiency of low level laser therapy in the treatment of oral lichen planus. A comparative evaluation of low-level laser and topical steroid therapies for the treatment of erosive-atrophic lichen planus. Open Access Maced J Med Sci 2015; 3: 717-21.
57. Mücke T, Genz I, Kanatas A, et al. Clinical trial analyzing the impact of continuous defocused CO2 laser vaporization on the malignant transformation of erosive oral lichen planus. J Cran Max-Fac Surg 2015; 43: 1567-70.
58. Munoz Sanchez PJ, Capote Femenias JL, Tuner J. Treatment of aphthous stomatitis using low-level laser therapy. Roots 2013; 4: 34-6.
59. Misra N, Chittoria N, Umapathy D, Misra P. Efficacy of diode laser in the management of oral lichen planus. BMJ Case Rep 2013; pii: bcr2012007609. doi: 10.1136/bcr-2012-007609.