Original Article

Clinical Evaluation of High and Low-Level Laser Treatment (CO_2*vs*InGaAlP Diode Laser) for Recurrent Aphthous Stomatitis

Nasim Zeini Jahromi [1], Janan Ghapanchi [1], Sara Pourshahidi [2], Maryam Zahed [1], Hooman Ebrahimi [3]

[1] Dept. of Oral and Maxillofacial Medicine, School of Dentistry, Shiraz University of Medical Sciences, Shiraz, Iran.
[2] Dept. of Oral and Maxillofacial Medicine, Tehran University of Medical Sciences, Tehran, Iran.
[3] Dept. of Oral Medicine, Dental School, Azad University, Tehran, Iran.

KEY WORDS
Aphthous;
Stomatitis;
Laser therapy;
Wound healing;

Received November 2015;
Received in Revised form February 2016;
Accepted May 2016;

ABSTRACT

Statement of the Problem: Recurrent aphthous stomatitis (RAS) is one of the most common lesions in the oral cavity. Due to its multifactorial nature, there is no definitive treatment for RAS. Laser therapy is one of the suggested treatments to reduce patient's discomfort.

Purpose: The purpose of the present clinical trial is to assess the effect of low and high level laser therapy on pain control and wound healing of RAS.

Materials and Method: Thirty six patients with minor RAS were divided into three groups. Group 1 (n=14) received CO_2 laser, group 2 (n=12) were treated with InGaAlP Diode laser and group 3 (n=10) received sham laser as placebo. All patients were evaluated daily up to 15 days after receiving one session of laser therapy. Pain severity before and after treatment, wound healing, patient's satisfaction, and functional disturbance before and after treatment were recorded for each patient.

Results: According to statistical analysis, pain reduction after treatment in group 1 was 7.00±2.41, in group 2 was 2.08±2.31, and in group 3 was 1.40±1.77. In addition, a significant difference was observed in the reduction of functional complications in CO_2 laser treated patients compared to the other two groups.

Conclusion: High-level laser treatment showed analgesic effects on RAS, but no healing was observed. Low-level laser therapy demonstrated no positive effect on recurrent aphthous ulcers.

Corresponding Author: Pourshahidi S., Dept. of Oral and Maxillofacial Medicine, Tehran University of Medical Sciences, Tehran, Iran. Tel: +98-2188015950 Email: p.oralmed@gmail.com

Cite this article as: Zeini Jahromi N., Ghapanchi J., Pourshahidi S., Zahed M., Ebrahimi H. Clinical Evaluation of High and Low-Level Laser Treatment (CO_2*vs*InGaAlP Diode Laser) for Recurrent Aphthous Stomatitis. *J Dent Shiraz Univ Med Sci.,* 2017 March; 18(1): 17-23.

Introduction

Recurrent aphthous stomatitis (RAS) is a common disorder of the oral cavity which affects 5-66% of adult patients and 20% of the general population. [1-2] The prevalence is higher among children and female patients. [3] The starting age seems to be between 10 to 19 years [4] and decreases in severity and frequency with aging. [5] Clinically, RAS is characterized by one or several recurrent painful ulcerations of the oral mucosa. [6] The lesion is a round or oval shallow ulcer with circumscribed erythematous margin and a yellow or gray base. [7] RAS has three different types: minor, major and herpetiform. [8] Even though a definitive etiologic factor(s) is not well understood for RAS, predisposing factors, such as age, gender, local conditions, systemic disorders, immunologic factors, psychological stress, medications, genetic, and microbial conditions are suggested to be involved. [9-12] Since the etiology is unknown, an approved curative therapy for RAS is lacking. Treatments are mostly nonspecific and often of limited efficacy. According to the literatures, available managements include topical agents like analgesics, antiseptics, corticosteroids, systemic therapy (such as pharmacologic therapy) and physical therapy, such as

surgical removal, debridement and laser application. [13-14] Laser is a unique form of energy which is widely used in medicine and dentistry due to its reparative, analgesic, and anti-inflammatory benefits. Different types of laser such as CO_2, Nd:YAG and InGaAlP Diode are used for treatment of complications on soft and hard tissues. High level lasers, such as CO_2 laser, have the possibility of using at high powers (ranging from fractions of a watt to 25 W or more), while low level lasers, such as InGaAlP Diode, operate in the milliwatt range(1-500 mW). Recently, several studies have revealed that low level laser therapy can be advantageous in the treatment of oral aphthous lesions by improving the process of wound healing and pain reduction and does not cause any serious adverse effect(s). [15-19] However, there appear to be few publications on the therapeutic effects of high level laser treatment on RAS. In view of the fact that RAS causes discomfort in patients and considering the potential therapeutic effects of laser on oral lesions, this study aimed to investigate and compare the efficacy of low and high level laser treatments on RAS in a randomized clinical trial.

Materials and Method

This study was designed as a randomized double-blind placebo-controlled clinical trial to evaluate the effect of low and high level laser therapy on RAS and comparing their efficacy. The study protocol was approved by the Ethics Committee of Shiraz University of Medical Sciences with the code number IRCT 2012120911702N1. The patients signed a consent form and were informed about the nature of the procedure before starting. Forty patients with aphthous lesions presented to the Oral and Maxillofacial Medicine Department of Shiraz Dental School between October 2012 and February 2013 voluntarily participated in the study. Patients were examined by a clinician and the diagnosis was confirmed through patient history and clinical examination. The inclusion criterion was patients with one minor RAS of less than 72 h duration or two nearby minor aphthous lesions of less than 72 h at the same side of oral cavity (the size of the two lesions plus the distance between them was not more than 9 mm). The exclusion criteria were patients who were not fulfilling the inclusion criteria, had serious and dangerous systemic diseases (including severe kidney, liver , and heart problems), pregnant and lactating women, patients treated with topical or systemic medication for RAS, such as corticosteroid therapy, antibiotics or analgesics during the previous month. Forty patients were divided into three groups with the method of simple randomization. The lesions of patients in group 1 were treated with CO_2 laser, those in group 2 were treated with InGaAlP Diode laser and the group 3 received sham laser (placebo group). Four of the patients (one from group1 and three from group 3) did not complete the procedure and were excluded from the study. The patients and the clinician who recorded the data were blind to the types of treatment applied.

The ulcers in group 1(n=14) were ablated with CO_2 laser (DEKA, 10600 nm) for about 5-10 seconds depending on the size of the lesion (scanning over the lesion until ablating the whole surface). The laser was irradiated with power output of 2W in continuous mode and the distance between the tissue and laser source was 12.5mm. In group 2 (n=12), InGaAlP Diode laser (AZOR-2K, 660nm) was emitted in pulse mode, frequency 80Hz, power output 25mW, power density 3J/cm², focal spot size 9.04mm for 4 minutes. The laser pen was in contact with the surface of the lesion. Group 3 (n=10) were treated with the low level laser (AZOR laser) inactive probe in contact with the lesion for 4 minutes. In all groups, no topical or injectable anesthesia was applied before the procedure and all patients received a single session treatment. The patients who had two ulcers at the same side were treated as same as the patients with single ulcer (the whole area of two ulcers were covered with the laser pen through only one application). Pain severity (both the idiopathic/ noncontact and contact pain) was evaluated with visual analogue scale (VAS) before and after treatment. Idiopathic or noncontact pain means the spontaneous pain which is felt by the patient without any stimulation of the ulcer. The patients' condition was followed up daily for 15 days after the treatment and their pain intensity was recorded using the VAS and the day in which the pain disappeared was noted. As the criteria for healing of the ulcer, we recorded the day in which the lesion was re-epithelialized while a remnant of lesion was still visible in clinical examination. We asked the patients about their satisfaction of the treatment and functional complications (interruption of the aphthous lesions with nor-

mal daily activities like speaking, chewing and brushing) before and after treatment. They were requested to grade these subjective data on a VAS. The collected data was analyzed statistically with Kruskal-Wallis, Mann-Whitney, Repeated measurement-one way ANOVA and Post Hoc Tests. The significant level (α) in this study was 0.05.

Results

In the present study, 38.8% (n=14) of the patients were in CO_2 laser group (group 1), 33.3% (n=12) received InGaAlP Diode laser therapy (group 2) and 27.7% (n=10) were in placebo group (group 3). The mean age of the patients in group 1, 2 and 3 was 34.6, 32.6 and 30.2, respectively. Group 1 consisted of 8 male and 6 female patients, group 2 involved 7 male and 5 female patients and group 3 comprised of 4 male and 6 female patients. There was no significant difference in the efficacy of therapies between genders.

The effect of the low and high level laser treatment on pain intensity was assessed using VAS and the results were compared to evaluate the efficiency of the investigated treatments. The difference between the three groups was not significant for idiopathic pain before and after treatment (p> 0.05).The contact pain reduction immediately after treatment in group1 was 7.00±2.41, in group2 was 2.08±2.31 and in group3 was 1.40±1.77.These results were significantly different between groups 1 and 2 (p= 0.000) and also groups 1 and 3 (p= 0.000).The difference in the reduction of post treatment contact pain; however, was not significant between groups 2 and 3 (p> 0.05).

Group1 experienced no pain 5.07±4.14 days after treatment, whereas group2 had no pain 3.00±2.08 days after laser therapy and group3 was pain free on the day 1.10±1.85. Statistically, group 1 patients experienced pain for a longer duration in comparison to the placebo group (p= 0.009). No significant difference was obtained between groups 1 and 2, as well as groups 2 and 3 (p> 0.05). Table 1 shows the percentage of pain free patients on different days after treatment in three groups.

Table 1: The percentage of pain free patients on different days in all groups

Pain cut (VAS=0)	Group 1	Group 2	Group 3
Day 1	21.40%	0	0
Day 3	42.80%	33.30%	33.30%
Day 7	71.40%	91.60%	91.60%
Day 10	85.70%	100%	100%
Day 12	100%		

VAS=visual analogue scale, Pain cut=the condition in which patients have no pain (VAS=0)

All the patients reported functional complications during chewing, brushing and even speaking. The functional disturbances before and after treatment were decreased by 8.57±1.50, 7.50±2.19 and 6.00±2.44 in group 1, 2 and 3, respectively. The difference was significant between groups 1 and 3 (p= 0.012), but statistically no reduction of functional disturbance was observed between groups 1 and 2, and also groups 2 and 3.

The comparison of the efficacy of the utilized lasers on the duration of ulcer repair showed no significant differences in the repair time of the lesions (p> 0.05) between the three groups. The percentages of healed ulcers of all groups on the follow-up days are demonstrated in Table 2. Statistically, the three groups revealed no satisfaction of laser treatment (p> 0.05).

Table 2: The percentage of healed ulcers on different days in all groups

Wound Healing	Group 1	Group 2	Group 3
Day 1	0	0	0
Day 3	14.20%	8.30%	10%
Day 7	57.10%	41.60%	80%
Day 9	71.40%	83.30%	100%
Day 14	85.70%	100%	
Day 15	100%		

The comparison of the clinical data and statistical analysis of the three groups are listed in Table 3.

Table 3: Comparison of pain reduction, pain cut, wound healing, patient´s satisfaction ,and decrease in functional complications

Variables	Group 1	Group 2	Group 3	P value
Idiopathic Pain Reduction	1.71±3.02	0.58±0.90	1.00±2.30	Not significant
Contact Pain Reduction	7.00±2.41	2.08±2.31	1.40±1.77	0.000
Pain Cut(Day)	5.07±4.14	3.00±2.08	1.10±1.85	0.012
Wound Healing(Day)	7.21±4.20	7.92±3.52	6.40±1.83	Not significant
Patient´s Satisfaction(VAS)	6.79±3.06	7.58±1.73	6.70±2.05	Not significant
Decrease in Functional Complications(VAS)	8.57±1.50	7.50±2.19	6.00±2.44	0.016

VAS=visual analogue scale, Pain cut (Day)=the day in which patients have no pain (VAS=0)

Discussion

Laser therapy is currently widely used in medical field due to its beneficial therapeutic effects, such as analgesia, anti-inflammation and wound healing. Although not completely known, laser therapy acts through different suggested mechanisms including modulation of natural substances (histamine, acetylcholine, opioid peptides, kinins, prostaglandin, interleukin, interferon and tumor necrosis factor), changes in impulse conduction of nociceptors and effects on lymphocyte metabolism. Laser therapy can also improve microcirculation and oxygenation of the tissue and stimulate epithelial, endothelial, and mesenchymal cell growth. [20-36]

In our study, we used CO_2 laser with 10600 nm, and 2 W parameters in continuous mode until ablating the whole ulcer and InGaAlP Diode laser, 660 nm, 25 mW and 3 J/cm^2 in pulse mode for 4 minutes. Laser was emitted for just one session in both groups. Results revealed that CO_2 laser was more effective in pain reduction in comparison to InGaAlP Diode laser and also the placebo group. The difference in pain reduction was not statistically significant between InGaAlP Diode laser and placebo group. Patients who were treated with CO_2 laser experienced more pain reduction immediately after treatment compared to the other two groups; however, they suffered from pain for a longer period of time. Statistically, the applied treatments in our study did not reduce the healing time of the lesions. CO_2 laser therapy resulted in decreasing the functional disturbances (speaking, chewing, and brushing), whereas InGaAlP Diode laser was not effective in pain and functional complication reduction. No visible side effect was observed during and after the laser therapy.

There are limited numbers of studies in which the effect of low and high level laser treatment on RAS were compared. De Souza *et al*. [37] has employed InGaAlP Diode laser (670 nm, 50 mW and 3 J/cm² in continuous mode) on minor RAS once per day until the ulcer disappeared and compared the laser therapy results with topical triamcinolone 4 times a day. InGaAlP Diode laser therapy had analgesic and healing effects in comparison to topical corticosteroid which is in contrast with the results of our present study. This discrepancy may be due to the difference laser power output, mode of laser irradiation and the number of treatment sessions between the studies. Khademi *et al*. [38] compared single-session InGaAlP Diode laser therapy (660 nm, 25 mW and 3 J/cm² in continuous mode) with placebo group. Their study showed reduction of pain and healing time after laser therapy, which may be due to the continuous mode of laser irradiation, which was the only difference between this study and our work. [38]

Zand *et al*. [39] suggested single-session CO_2 laser therapy for minor RAS. They applied the laser in non-thermal way with the power of 1 W. [39] Similar to our study, CO_2 laser treatment reduced pain immediately after irradiation in comparison to placebo. The results which were reported by Sharon-Bulle *et al.* [40] and Colvard *et al*. [41] using CO_2 laser in ablative manner are in agreement with our study. More recently, Zand *et al*. [42] evaluated non-thermal non-ablative 1 W CO_2 laser on wound healing of minor RAS for one session. Their study revealed that laser treatment can improve healing of the ulcers which is in contrast to our results. [42] The use of the non-ablative method in this study may explain the different results obtained compared to ours.

Tezel *et al*. [43] and Arabaci *et al*. [44] compared the effects of Nd:YAG laser (1.064 nm, power output 2W) with topical corticosteroid (triamcinolone acetonide 0.1%). Both of them reported more pain reduction after Nd:YAG laser treatment and fewer functional complications in consistent with our study, but faster healing and better patient acceptance with laser which was not appeared significant in ours. The study by Parkins [45] demonstrated immediate pain reduction and faster healing after Nd:YAG laser application on aphthous lesions. Employing a different type of laser in these studies may explain the inconsistency which was observed between the aforementioned results and the present study.

Concerning a few limitations in our study, it would be ideal to conduct this type of study with patients having multiple simultaneous lesions in their oral cavity and to compare the effect of different laser types on the same person; however, it was not possible to find enough patients having this condition and also fulfilling our inclusion criteria. It is noteworthy to mention that RAS has a recurrent nature; therefore, further studies are required to evaluate the effect of laser therapy on the recurrence of aphthous lesions.

Generally, our study showed that high level laser

treatment of RAS could significantly reduce the pain and decrease the functional disturbances in patients with a single treatment session and more importantly, these benefits occurred immediately after the treatment. Since RAS causes discomfort in patients and has a recurrent nature, this type of therapy can be extremely invaluable to patients. Certainly, more controlled clinical trials are required to establish an ideal protocol for the use of lasers in the treatment of oral lesions.

Conclusion

CO_2 laser reduced pain intensity of RAS immediately after treatment, although the pain remained longer after this type of laser treatment in comparison to InGaAlP Diode laser. CO_2 laser treatment also resulted in fewer functional complications in comparison to placebo group. The investigated laser therapies could not significantly reduce the wound healing time.

Acknowledgements

The authors thank the Vice-Chancellery of Shiraz University of Medical Sciences, for supporting the research (Grant# 90-01-03-4105). This article is based on the thesis by Dr. Nasim Zeini Jahromi. The authors also thank Dr. Mehrdad Vossoughi of the Dental Research Development Center of the School of Dentistry, for the statistical analysis.

Conflict of Interest

There is no Conflict of Interest pertaining to any of the authors.

References

[1] Porter SR, Hegarty A, Kaliakatsou F, Hodgson TA, Scully C. Recurrent aphthous stomatitis. Clin Dermatol. 2000; 18: 569-578.

[2] Rennie JS, Reade PC, Hay KD, Scully C. Recurrent aphthous stomatitis. Br Dent J. 1985; 159: 361-367.

[3] Chavan M, Jain H, Diwan N, Khedkar S, Shete A, Durkar S. Recurrent aphthous stomatitis: a review. J Oral Pathol Med. 2012; 41: 577-583.

[4] Ship JA, Chavez EM, Doerr PA, Henson BS, Sarmadi M. Recurrent aphthous stomatitis. Quintessence Int. 2000; 31: 95-112.

[5] Rogers RS 3rd. Recurrent aphthous stomatitis: clinical characteristics and associatedsystemic disorders. Semin Cutan Med Surg. 1997; 16: 278-283.

[6] Graykowski EA, Barile MF, Lee WB, Stanley HR Jr. Recurrent aphthous stomatitis. Clinical, therapeutic, histopathologic, and hypersensitivity aspects. JAMA. 1966; 196: 637-644.

[7] Jurge S, Kuffer R, Scully C, Porter SR. Mucosal disease series. Number VI. Recurrent aphthous stomatitis. Oral Dis. 2006; 12: 1-21.

[8] Stanley HR. Aphthous lesions. Oral Surg Oral Med Oral Pathol. 1972; 33: 407-416.

[9] Ship JA. Recurrent aphthous stomatitis. An update. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 1996; 81: 141-147.

[10] Woo SB, Sonis ST. Recurrent aphthous ulcers: a review of diagnosis and treatment. J Am Dent Assoc. 1996; 127: 1202-1213.

[11] Soto Araya M, Rojas Alcayaga G, Esguep A. Association between psychological disorders and the presence of Oral lichen planus, Burning mouth syndrome and Recurrent aphthous stomatitis. Med Oral. 2004; 9: 1-7.

[12] Natah SS, Konttinen YT, Enattah NS, Ashammakhi N, Sharkey KA, Häyrinen-Immonen R. Recurrent aphthous ulcers today: a review of the growing knowledge. Int J Oral Maxillofac Surg. 2004; 33: 221-234.

[13] Field EA, Allan RB. Review article: oral ulceration--aetiopathogenesis, clinical diagnosis andmanagement in the gastrointestinal clinic. Aliment Pharmacol Ther. 2003; 18: 949-962.

[14] Khoo SP. Management Of Oral Recurrent Aphthous Stomatitis (ORAS). Annal Dent Univ Malaya. 1999; 6: 40-42.

[15] Myers TD, McDaniel JD. The pulsed Nd:YAG dental laser: review of clinical applications. J Calif Dent Assoc. 1991; 19: 25-30.

[16] Pereira LB, Chimello DT, Ferreira MR, Bachmann L, Rosa AL, Bombonato-Prado KF. Low-level laser therapy influences mouse odontoblast-like cell response in vitro. Photomed Laser Surg. 2012; 30: 206-213.

[17] Marques MM, Pereira AN, Fujihara NA, Nogueira FN, Eduardo CP. Effect of low-power laser irradiation on protein synthesis and ultrastructure of human gingival fibroblasts. Lasers Surg Med. 2004; 34: 260-265.

[18] Colvard M, Kuo P. Managing aphthous ulcers: laser treatment applied. J Am Dent Assoc. 1991; 122: 51-53.

[19] Prikuls VF. Experience in irradiating with helium-neon lasers to treat patients withrelapsing aphthous stomatitis. Stomatologiia (Mosk). 2000; 79: 20-22.

[20] Wesselmann U, Lin SF, Rymer WZ. Selective decrease of small sensory neurons in lumbar dorsal root ganglia labeled with horseradish peroxidase after ND:YAG laser irradiation of the tibial nerve in the rat. Exp Neurol. 1991; 111: 251-262.

[21] Kasai S, Kono T, Yamamoto Y, Kotani H, Sakamoto T, Mito M. Effect of low-power laser irradiation on impulse conduction inanesthetized rabbits. J Clin Laser Med Surg. 1996; 14: 107-109.

[22] Orchardson R, Peacock JM, Whitters CJ. Effect of pulsed Nd:YAG laser radiation on action potential conduction in isolated mammalian spinal nerves. Lasers Surg Med. 1997; 21: 142-148.

[23] Mizutani K, Musya Y, Wakae K, Kobayashi T, Tobe M, Taira K, et al. A clinical study on serum prostaglandin E2 with low-level laser therapy. Photomed Laser Surg. 2004; 22: 537-539.

[24] Convissar RA, Massoumi-Sourey M. Recurrent aphthous ulcers: etiology and laser ablation. Gen Dent. 1992;40: 512-515.

[25] Pick RM, Colvard MD. Current status of lasers in soft tissue dental surgery. J Periodontol. 1993; 64: 589-602.

[26] Enwemeka CS, Parker JC, Dowdy DS, Harkness EE, Sanford LE, Woodruff LD. The efficacy of low-power lasers in tissue repair and pain control: a meta-analysis study. Photomed Laser Surg. 2004; 22: 323-329.

[27] Bortone F, Santos HA, Albertini R, Pesquero JB, Costa MS, Silva JA Jr. Low level laser therapy modulates kinin receptors mRNA expression in the subplantar muscle of rat paw subjected to carrageenan-induced inflammation. Int Immunopharmacol. 2008; 8: 206-210.

[28] Mafra de Lima F, Costa MS, Albertini R, Silva JA Jr, Aimbire F. Low level laser therapy (LLLT): attenuation of cholinergic hyperreactivity, beta(2)-adrenergic hyporesponsiveness and TNF-alpha mRNA expressionin rat bronchi segments in E. coli lipopolysaccharide-induced airway inflammation by a NF-kappaB dependent mechanism. Lasers Surg Med. 2009; 41: 68-74.

[29] Eduardo FP, Mehnert DU, Monezi TA, Zezell DM, Schubert MM, Eduardo CP, et al. Cultured epithelial cells response to phototherapy with low intensitylaser. Lasers Surg Med. 2007; 39: 365-372.

[30] Simunovic Z, Ivankovich AD, Depolo A. Wound healing of animal and human body sport and traffic accidentinjuries using low-level laser therapy treatment: a randomized clinical study of seventy-four patients with control group. J Clin Laser Med Surg. 2000; 18: 67-73.

[31] Kreisler M, Christoffers AB, Al-Haj H, Willershausen B, d'Hoedt B. Low level 809-nm diode laser-induced in vitro stimulation of the proliferation of human gingival fibroblasts. Lasers Surg Med. 2002; 30: 365-369.

[32] Safavi SM, Kazemi B, Esmaeili M, Fallah A, Modarresi A, Mir M. 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. 2008; 23: 331-335.

[33] Almeida-Lopes L, Rigau J, Zângaro RA, Guidugli-Neto J, Jaeger MM. Comparison of the low level laser therapy effects on cultured humangingival fibroblasts proliferation using different irradiance and same fluence. Lasers Surg Med. 2001; 29: 179-184.

[34] Pereira AN, Eduardo Cde P, Matson E, Marques MM. Effect of low-power laser irradiation on cell growth and procollagen synthesis of cultured fibroblasts. Lasers Surg Med. 2002; 31: 263-267.

[35] Mester E, Mester AF, Mester A. The biomedical effects of laser application. Lasers Surg Med. 1985; 5: 31-39.

[36] Longo L, Evangelista S, Tinacci G, Sesti AG. Effect of diodes-laser silver arsenide-aluminium (Ga-Al-As) 904 nm on healing of experimental wounds. Lasers Surg Med. 1987; 7: 444-447.

[37] De Souza TO, Martins MA, Bussadori SK, Fernandes KP, Tanji EY, Mesquita-Ferrari RA, et al. Clinical evaluation of low-level laser treatment for recurring aphthous stomatitis. Photomed Laser Surg. 2010; 28 Suppl 2: S85-S88.

[38] Khademi H, Shirani A, Nikeghbal F. Evaluation of the effect of low level laser on Recurrent Aphtous Stomatitis. J Dent Shiraz Univ Med Scien. 2009; 10 Suppl 2: 159-161.

[39] Zand N, Ataie-Fashtami L, Djavid GE, Fateh M, Alinaghizadeh MR, Fatemi SM, et al. Relieving pain in minor aphthous stomatitis by a single session of non-thermal carbon dioxide laser irradiation. Lasers Med Sci. 2009; 24: 515-520.

[40] Sharon-Buller A, Sela M. CO2-laser treatment of ulcerative lesions. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 2004; 97: 332-334.

[41] Colvard M, Kuo P. Managing aphthous ulcers: laser treatment applied. J Am Dent Assoc. 1991; 122: 51-53.

[42] Zand N, Fateh M, Ataie-Fashtami L, Djavid GE, Fatemi SM, Shirkavand A. Promoting wound healing in minor recurrent aphthous stomatitis by non-thermal, non-ablative

CO(2) laser therapy: a pilot study. Photomed Laser Surg. 2012; 30: 719-723.

[43] Tezel A, Kara C, Balkaya V, Orbak R. An evaluation of different treatments for recurrent aphthous stomatitisand patient perceptions: Nd:YAG laser versus medication. Photomed Laser Surg. 2009; 27: 101-106.

[44] Arabaci T, Kara C, Ciçek Y. Relationship between periodontal parameters and Behçet's disease andevaluation of different treatments for oral recurrent aphthous stomatitis. J Periodontal Res. 2009; 44: 718-725.

[45] Parkins F. Lasers in pediatric and adolescent dentistry. Dent Clin North Am. 2000; 44: 821-830.