The Effect of Carbon Dioxide Laser on Aphthous stomatitis Treatment: A Double-Blind Randomized Clinical Trial

Seyyed Amir Seyyedi¹, Pooya Olyaei², Reza Fekrazad³, Sanaz Partovi⁴, Maryam Baghizadeh Fini^{5,6*}

¹Faculty of Dentistry, Urmia University of Medical Sciences, Urmia, Iran

²Implantology, Urmia University of Medical Sciences, Urmia, Iran

³Faculty of Dentistry, AJA University of Medical Sciences, Tehran, Iran

⁴Urmia University of Medical Sciences, Urmia, Iran

⁵School of Dentistry, Tehran University of Medical Sciences, Tehran, Iran

⁶Health Promotion, Oklahoma State University, Stillwater, OK, USA

*Correspondence to

Maryam Baghizadeh Fini; DDS,
School of Dentistry, Tehran
University of Medical Sciences,
Tehran, Iran.

Master's Student, Master of
Health Promotion, Oklahoma
State University, Stillwater, OK,
USA. Tel: +1 (405) 612-1737;
Email: m.baghizadeh92@gmail.
com

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Abstract

Introduction: This randomized clinical trial was designed to investigate the effect of carbon dioxide laser on the treatment of minor recurrent aphthous stomatitis (miRAS) as a painful and common oral ulcer.

Methods: Fifteen patients with miRAS entered into this study after compliance with the inclusion and exclusion criteria. The patients were assigned to three groups of pulsed CO₂ laser, continuous CO₂ laser, and control. A pulsed CO₂ laser with power of 261 W and pulse duration of 180 microseconds and continuous CO₂ lasers with the power of 1 W and radiation duration of 5-10 seconds were used. In the control group, topical triamcinolone ointment of 0.1% was used. The degree of pain was measured using the visual analogue scale (VAS). The patients were evaluated in terms of pain intensity before and immediately after the treatment and at follow-up hours, 12, 24, 48, and 72 hours after the intervention, and changes in the size of the ulcers were measured before the treatment and on third, fifth, and seventh days.

Results: The effect of CO₂ laser with pulsed and continuous radiation on the pain intensity of aphthous lesions, immediately after the treatment and at subsequent follow-up hours were similar and even better than the control group ($P < 0.05$). All three treatments had a similar effect on the size of the ulcer, which was not statistically significant ($P > 0.05$).

Conclusion: The results of this randomized controlled trial (RCT) showed that the carbon dioxide laser, whether with pulsed radiation or continuous radiation compared to the control group, had a better impact on the pain relief of aphthous lesions.

Keywords: Recurrent aphthous stomatitis; Laser; Carbon dioxide lasers; Pain.

Introduction

Recurrent aphthous stomatitis (RAS) is a common and recurrent disease diagnosed with recurrent ulcers limited to oral mucosa in patients who have no other signs of systemic disease.^{1,2} RASs are painful, round, or elliptical ulcers recurring at different intervals. These ulcers include a central necrotic part with fibrinous and whitish gray exudate and a red halo is around it.^{1,3,4}

Recurrent aphthae are observed in three forms of minor, major, and herpetic aphthae.^{1,4,5} Minor recurrent aphthae are the most common form (80%-90%) of the disease and the patient has a history of former aphthae,² usually healed during 7-10 days without a scar. Their size is 2-4 mm (less than 1 cm) on average and the most prevalent place of involvement is buccal and labial mucosa.^{6,7} Aphthous stomatitis is the most common ulcerative

disease of the oral mucosa.^{8,9} The prevalence reported in the normal population in the world is between 5% and 66% with the mean of 20%⁵ and the prevalence is 25.2% in Iran.¹⁰ The prevalence of the disease in people with a higher social-economical level is more than others and that amount in females is observed slightly more than in males.³ There is no relationship between the pain degree of aphthous lesions and the size of the lesions and it can be very intensive in such a way that it may disrupt one's eating, drinking, and even talking.^{2,11}

Because there is no agreement on the cause of the aphthae, it is difficult to find an effective treatment for it. Therefore, three goals are followed in the treatment of recurrent aphthous stomatitis: patient's pain control, accelerated ulcer healing, and reduced recurrence of lesions. Different drugs and treatments are used to reduce

the pain of aphthous stomatitis, including mouthwashes, antibiotics, topical anesthetics, using silver nitrate pen, and cryotherapy.¹¹⁻¹⁴ In most of the patients, the main pivot of the treatment is topical and systemic corticosteroids which have complications such as weakening the immune system and reducing the barrier defenses of the body against a variety of infections, delaying the ulcer healing, reducing and weakening of the mucous membranes of the gastrointestinal system, especially the stomach, which causes and exacerbates the gastrointestinal ulcers.¹⁵

Another therapeutic option for this complication is laser treatment that seems to be effective in reducing pain intensity, inflammation and edema, accelerating ulcer healing, and improving the depth of the tissues and nerves. These effects in low-power lasers result from the changes that happened due to the laser therapy in the cellular mechanism.¹⁶⁻¹⁹

Lasers used to treat aphthous lesions include InGaAlP, Nd: YAG, CO₂ and diode lasers²⁰⁻²⁴ among which the CO₂ laser is superior to other types of lasers due to its simultaneous effects on pain and aphtha healing time and its very low power with low radiation duration and it can therefore be effective in the treatment of recurrent aphthous stomatitis.²⁰ The CO₂ laser with a 10600 nm wavelength is used to treat oral aphthous lesions with different average power of 0.7 W,²⁵ 1 W,^{2, 26} 2 W^{23,27} and 3 W²⁸ continuously with^{28,29} or without local anesthesia^{26, 30} beyond the clear gel.^{2,26,27}

The present study was designed and performed to review the effect of a session of using carbon dioxide laser on pain and size of minor aphthous lesions and compare its effects with the control group.

Materials and Methods

Study Plan

This randomized and interventional clinical trial study was done on patients referred to the clinics and offices in Urmia after obtaining permission from the Ethics Committee of Urmia University of Medical Sciences. This clinical trial was registered in the Iranian Registry of Clinical Trials (IRCT) with code IRCT20180224038840N1. Fifteen people who had a clinical diagnosis of minor RAS (miRAS) with a detailed history and examination by a knowledgeable clinician were selected. For all patients, the usual clinical and paraclinical procedures took place to reject the underlying causes. Then, the patients entered into the study after compliance with the inclusion and exclusion criteria.^{6,7,24,25} The inclusion criteria were:

1. A definitive diagnosis of minor aphthous stomatitis,
2. It should be less than 72 hours after lesions form,
3. The diameter of the lesions is less than 10 mm.

Exclusion criteria include:

1. Underlying systemic problems (such as anemia, diabetes, pregnancy),
2. Atypical cases of aphtha and suspected cases of Behçet's syndrome, inflammatory bowel diseases, etc,

3. Simultaneous use of any type of topical drugs for aphtha treatment,
4. Using any type of topical or systemic anesthetic compounds before laser irradiation, during it and within 4 days in follow-up,
5. Using any kind of systemic treatment of aphtha during three previous months,
6. Age less than 12 years.

Before the treatment, the research nature of the protocol and the implementation of the protocol were described for the patient and informed consent was obtained.

Intervention

In the first session, the initial examination was performed by a general dentist. In this session, the history of medicine use, previous lesions, and various diseases such as gastrointestinal diseases, blood diseases, and skin diseases was obtained. The size of the lesions was measured and recorded by a periodontal probe. Paraclinical tests including complete blood count (CBC), fasting blood sugar (FBS), ferritin, and thyroid stimulating hormone (TSH) were conducted.

The patients were randomly divided into three groups of 5: patients of the pulsed laser as group A, patients of the continuous laser as group B, and the control group as group C. The randomizing operation was done confidentially and at a site outside the center by the block randomization method.

In the patients of laser groups, before starting laser therapy on aphthous lesions, a layer of 3 mm thick transparent gel (Lubricating Jelly, Abzar Darman Co., Iran) which contains a high amount of water (87.5%) without any topical anesthetic property was placed. Before the start of radiation, the patient and staff of the operating room put on safety goggles which are appropriate to the wavelength of the CO₂ laser (10600 nm). For those lesions using the continuous laser, lesions were treated by the laser with a power of 1 W above the gel layer. The radiation duration was 5 to 10 seconds and the radiation method was spiral. In the type of pulsed radiation, the power of the laser was 261 W, pulse duration was 180 microseconds and the pulses interval was 40 milliseconds. The laser used in the above-mentioned groups was Ultra-Dream Daeshin Enterprise, model: DS-40U type, made in South Korea with a wavelength of 10600 nm and maximum power of 315 W. Given the presence of laser therapy, there was no need for topical or systemic anesthetics. In the control group, oral ointment of 0.1% triamcinolone acetonide (Teriagent, Raha Pharmaceutical Co., Iran) was used. This ointment was applied by the patient in the aphthous lesion area using a special daily applicator, four times after meals and before bedtime.

Before, immediately after and 12, 24, 48, and 72 hours after the treatment, pain intensity was evaluated by the patients based on VAS criteria in which score 0 means no pain and 10 means maximum and intolerable pain. In

the follow-up on the third, fifth, and seventh day after the treatment, due to self-limiting conditions, fatigue, loss, and healing within 10-14 days, the patient was examined at the office by the project executor who was not aware of group types. At these sessions, the size of the aphthous lesions was measured in millimeters with a periodontal probe and was compared to the size of the lesion before the treatment.

Laser therapy was performed for patients by a laser fellowship with the same condition. The amount of pain and size of the lesions after laser treatment was checked by an examiner (general dentist) who was unaware of the type of treatment and the type of grouping. The statistician who performed the analyses of this study was also unaware of the treatments and the type of patients' grouping. Since both the examiner and the statistician were non-informative, our study is a double-blind study.

Statistical Analysis

Obtained data were analyzed by SPSS 20 software. The results were expressed as mean $\pm$ standard deviation. Statistical evaluation was reviewed using tests of repeated measurement ANOVA and one-way ANOVA. *P* values less than 0.05 in a two-range test were considered significant.

Results

Fifteen patients (13 females and 2 males) who had 15 minor aphthous lesions were selected and remained in the plan until the end of the study. The mean age of the patients was 34.54 ± 14.93 years (17-60 years old) (Figure 1).

The comparison of pain intensity average before the treatment in the studied groups, including the pulsed carbon dioxide laser, the continuous carbon dioxide

Figure 1. The Age Average of Patients in Three Different Groups.

laser, and the control group, showed the pain intensity average between groups was different, although this difference was not statistically significant (*P* value > 0.05). The comparison of pain intensity average before the intervention with time intervals of measurement pain intensity after the intervention showed in the pulsed and continuous CO₂ laser groups, there is also a statistically significant difference between mean $\pm$ observed standard error before the intervention and after the intervention including all time-intervals of measurement (immediately after the intervention, 12, 24, 48 and 72 hours after the intervention). In the control group, the difference of mean $\pm$ standard error of pain intensity between time-intervals before the intervention and time-intervals immediately after the intervention and 72 hours after the intervention was significant. However, the difference in pain intensity average between time-intervals before the intervention and the time-intervals of 12, 24, and 40 hours after the intervention was not statistically significant (Figure 2 and Table 1).

Comparing the mean size of the ulcer at the measured time intervals in the studied groups showed the average

Table 1. Comparison of Pain Intensity Average Between Before Intervention and Time of Pain Evaluation After Intervention in Each Group

Group	Time of Pain Evaluation	Mean Difference $\pm$ Standard Error	P Value
Pulsed CO ₂ laser	Right after intervention	4.6 $\pm$ 0.68	0.002
	12 hours	4.4 $\pm$ 0.4	<0.001
	24 hours	4.6 $\pm$ 0.4	<0.001
	48 hours	3.4 $\pm$ 0.93	0.021
	72 hours	4.4 $\pm$ 1.08	0.015
Continuous CO ₂ laser	Right after intervention	4.6 $\pm$ 0.98	0.009
	12 hours	3.4 $\pm$ 0.93	0.021
	24 hours	3.4 $\pm$ 0.93	0.021
	48 hours	4 $\pm$ 1.05	0.019
	72 hours	4.8 $\pm$ 0.38	<0.001
Usual treatment	Right after intervention	1.8 $\pm$ 0.49	0.021
	12 hours	2.4 $\pm$ 1.03	0.08
	24 hours	2.6 $\pm$ 0.98	0.057
	48 hours	3.4 $\pm$ 1.4	0.072
	72 hours	4 $\pm$ 1.3	0.037

Figure 2. Comparison of the Pain Intensity Mean at Measured Time-Intervals in Three Studied Groups.

Figure 3. Comparison of the Mean Ulcer Size at Measured Time-Intervals in Three Studied Groups.

size of the ulcer on the first day in the pulsed CO₂ laser group was higher than the other two groups; however, the observed difference was not statistically significant (P value = 0.93). Comparing the mean ulcer diameter difference on the first day with the intervals of the third, fifth and seventh days in the pulsed carbon dioxide laser group revealed that the difference between the mean $\pm$ standard error of the ulcer size on the first day and those on the third and fifth days was not significant. However, the mean difference between the first and seventh days was significant. In the continuous CO₂ laser group, comparing the mean ulcer diameter difference on the first day with the third day was not significant, while the difference in the average diameter of the lesion on the first day with the fifth and seventh days was significant. In the control group, the observed results comparing the first day with the third day were meaningless, and in comparison with the first day and the fifth and seventh days they were meaningful (Figure 3 and Table 2).

Discussion

The results of this study approve a significant pain reduction in patients with RAS because of using pulsed and continuous CO₂ lasers in comparison with the control

group. In various studies that have investigated the effect of lasers on aphthous ulcers in the mouth, other types of lasers have also been used. The difference in the type of lasers used is in the properties of the laser protocol (power, dose, wavelength, time of examination after the laser). In the present research, the reduction of pain in patients with recurrent oral aphthous ulcers was observed immediately after the laser and at follow-up hours, 12, 24, 40, and 72 hours after the intervention. Zand et al showed the effect of the continuous CO₂ laser with the power of 1 W in immediate pain reduction in follow-up hours, 4, 8, 12, 24, 40, 72, and 96 hours after the treatment.²

Sharon-Buller and Sela reported a case of using a CO₂ laser for pain relief of recurrent aphthous lesions in a 50-year-old patient. Using a CO₂ laser with a wavelength of 10600 nm and power of 1-1.5 W and the radiation duration of 5 seconds without topical anesthesia, she reported an immediate and prolonged pain reduction of the lesion.³⁰ In a study by Zeini Jahromi et al, the evaluating effects of the continuous CO₂ laser in comparison with the diode laser and silent laser on recurrent aphthous stomatitis indicated that patients in the group of continuous CO₂ lasers with power of 2 W compared to patients in the other two groups experienced

Table 2. Comparison of Lesion Size Average in Time of Pain Evaluation in Each Group

		Pulsed CO ₂ Laser	Continuous CO ₂ Laser	Usual Treatment	P Value
Mean $\pm$ Standard Deviation					
Lesion size	day 1	4.17 $\pm$ 1.94	3.9 $\pm$ 2.07	3.8 $\pm$ 0.84	0.93
	day 3	4 $\pm$ 1.18	3.7 $\pm$ 2.22	3 $\pm$ 1.6	0.67
	day 5	2.42 $\pm$ 2.11	1.4 $\pm$ 2.2	0.8 $\pm$ 0.84	0.37
	day 7	1.17 $\pm$ 1.81	0.6 $\pm$ 1.34	0 $\pm$ 0	0.4
	P value inside the groups	0.02	<0.001	<0.001	
Mean $\pm$ Standard Error					
Total		2.94 $\pm$ 0.61	2.4 $\pm$ 0.67	1.9 $\pm$ 0.67	0.53

significant reduction in pain intensity. However, in terms of healing time, satisfaction, and daily dysfunction, no significant difference was observed in different groups.²³ In the present study, about changing the size of RAS ulcers following the treatment in the three control groups on third, fifth and seventh days after the treatment in comparison with before the treatment, there was no significant difference. In a study by Prasad and Pai using a continuous CO₂ laser with the power of 0.7 W, lesion healing was studied on days 3 and 4 after the treatment and every two days for up to two weeks. The reduction of the erythematous halo around the aphtha and the complete ulcer removal meant to be aphtha healing. The results of this study showed the duration of ulcer healing in the laser group was shorter than that of the placebo group.²⁵ This difference in the present study can be due to different average power and hours of follow-up and also the difference in the indicator of ulcer healing. The results of this clinical trial showed that the carbon dioxide laser, whether with continuous radiation or pulsed radiation, can be used to relieve the pain of minor aphthous lesions.

The high cost of laser therapy was one of the limitations of our study, but no cost was incurred by the patients in this regard.

Ethical Considerations

This randomized and interventional clinical trial study was done on patients referred to the clinics and offices in Urmia after obtaining permission from the Ethics Committee of Urmia University of Medical Sciences with IR.UMSU.Rec.1396.364 registration number, and written informed consent was obtained from all the patients.

Conflict of Interests

The authors declare that they have no conflict of interest.

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