

# CO<sub>2</sub> Laser Management of Leukoplakias: A Clinical Follow-up

Sebnem Ercalik Yalcinkaya<sup>a</sup>, Asim Dumlu<sup>b</sup>, Vakur Olgac<sup>c</sup>, Semih Ozbayrak<sup>d</sup>

<sup>a</sup> Resident, Department of Oral Diagnosis and Radiology, Faculty of Dentistry, Marmara University, Istanbul, Turkey.

<sup>b</sup> Associate Professor, Department of Oral Diagnosis and Radiology, Faculty of Dentistry, Marmara University, Istanbul, Turkey.

<sup>c</sup> Resident, the Department of Pathology, Oncology Institute, Istanbul University, Istanbul, Turkey.

<sup>d</sup> Professor and Head of Department of Oral Diagnosis and Radiology, Faculty of Dentistry, Marmara University, Istanbul, Turkey.

**Purpose:** To clinically evaluate the effectiveness of CO<sub>2</sub> laser in oral leukoplakia cases.

**Materials and Methods:** Twenty-two cases of oral leukoplakia, both clinically and histologically diagnosed in 14 patients, were successfully treated with CO<sub>2</sub> laser with focus probe, in continuous operating mode at 5 to 8 W. Oral smears were obtained throughout the follow-up to determine whether there was any dysplastic alteration.

**Results:** The healing was ensured by secondary epithelialization. The treated areas appeared normal within 3 to 5 weeks after performing one-step laser surgery. The follow-up period has been continuing for 5 years. To date, recurrence has been seen in one patient. No patient showed any sign of dysplasia or neoplasia during the follow-up.

**Conclusion:** Since CO<sub>2</sub> laser penetration into tissue provides the best results when treating superficial lesions, the CO<sub>2</sub> laser appears to have an important place in the effective management of leukoplakia.

**Key words:** CO<sub>2</sub> laser, oral leukoplakia.

*J Oral Laser Applications 2005; 5: 91-102.*

*Submitted for publication:24.10.04; accepted for publication:4.02.05.*

Leukoplakias are white patches that cannot be wiped off the mucosa and that have no identifiable etiology. They are differentiated into homogeneous and nonhomogeneous forms. The main predisposing factors for the development of oral leukoplakias are smoking and alcohol consumption. Physical irritants, galvanism, chronic trauma, poor oral hygiene, *Candida albicans*, and human papilloma virus (HPV) have also been incriminated.<sup>1-5</sup>

Silverman et al<sup>6</sup> conducted a follow-up study of 257 patients, estimating the average malignant transformation rate of leukoplakia to be 5% to 6% or more depending on the time of observation. Currently, dysplasia appears to be the best predictor of malignant potential. Dysplastic lesions do not have any specific clinical appearance. In any case, the clinical appearance is not indicative of the histology.<sup>3-6</sup>

The first step in the management of oral leukoplakia is in the elimination of all possible predisposing etiological factors. Therapeutic procedures are not yet standardized, even if most authors agree that the surgical approach is the most effective therapy. If the lesion is small, excisional biopsy is recommended. It is advisable to perform incisional biopsy of larger lesions for histopathological evaluation that will guide further decisions on the treatment.<sup>7</sup> Alternatives to scalpel or standard excisional surgery are cryosurgery<sup>8</sup> and laser ablation.<sup>9-15</sup>

Homogeneous leukoplakias representing moderate to severe epithelial dysplasia should always be removed either by conventional or CO<sub>2</sub> laser surgery.<sup>9-12</sup> Other treatment modalities include cryosurgery and electrodesiccation, which are usually ineffective.<sup>3,4</sup>

Since recurrences are relatively common in oral leukoplakia, the patients should be examined periodically.<sup>3,13</sup>

The purpose of this study was to evaluate the long-term clinical effects of CO<sub>2</sub> laser management and the probability of developing local recurrences and/or precancerous change of oral leukoplakias in a 5-year follow-up period.

## MATERIALS AND METHODS

Fourteen patients (9 male, 5 female; aged 44 to 65 years) bearing 22 oral leukoplakias were involved in this study. The patients were instructed on the nature of the treatment, and any suspected causal factors were corrected. Patients were informed that tobacco and alcohol habits should cease. The preoperative evaluation included a careful examination and photographs of the lesion.

In all cases, the relative risk of malignant potential was determined by the presence of epithelial dysplasia in cytological and histological examinations. Smears were obtained by means of a Cytobrush cell collector (Cytobrush, GT, Med-Scand Medical, Malmö, Sweden) and were fixed immediately with Mercifix spray (Merck, Darmstadt, Germany). Histological examinations were done by incisional scalpel biopsy.

The treatment was conducted under local anesthesia (4% Prillocaine HCl or 2% Articaine HCl) with a CO<sub>2</sub> laser (Sharplan 15 F, Tel Aviv, Israel) operating at 200 to 240 V (50 to 60 Hz), with a 0.4-mm spot size in noncontact mode. The laser wavelength was 10.6 μm (infrared), and it was continuously adjustable from 1 to 15 W.

The necessary safety rules were followed, and non-reflective handpieces were used during the treatment. The CO<sub>2</sub> laser treatment was performed in continuous operating mode (cw) between 5 (860 J/cm<sup>2</sup>) and 8 W (1376 J/cm<sup>2</sup>) according to manufacturer's recommendation and treatment needs of the patients. Straight or 110-degree contra-angled focusing handpieces with an air-cooling function were used to access the different areas. As a means of cleaning away the carbonized layer, the mouth was wiped with gauze. Consequently, remaining areas were detected and eliminated.

Healing was achieved by secondary epithelialization. In order to reduce the patient's sensitivity during the healing process, an anesthetic mouthwash composed of 0.15% benzydamine hydrochloride was prescribed for all patients 4 times/day for 4 days. In addition, to speed up the epithelization process, the patients were

given 100 mg Dekspanthenol pastilles (Roche, Istanbul, Turkey) to be taken 6 times/day for 1 week.

Each site was treated in a one-step procedure. The treated sites were examined on the 7th, 15th, and 21st day postoperatively, and again after 4, 5, 10, and 20 weeks for treatment response and complications. They have been recalled every 6 months for 5 years.

## RESULTS

Age, gender, habits of the patients, location of the lesions, the power of the CO<sub>2</sub> laser during the procedures, duration of epithelialization, keratinization, and recurrence are shown in Table 1.

In terms of alcohol and smoking habits, 7 of the 14 patients were mainly smokers only (50%). Five patients consumed both tobacco and alcohol (35.8%). Two of the 14 patients were ex-smokers (14.2%). In spite of being told to stop smoking and/or drinking habits, only 5 patients modified their smoking habits, while 1 of the 4 heavy drinkers stopped drinking through attending a program for alcoholics.

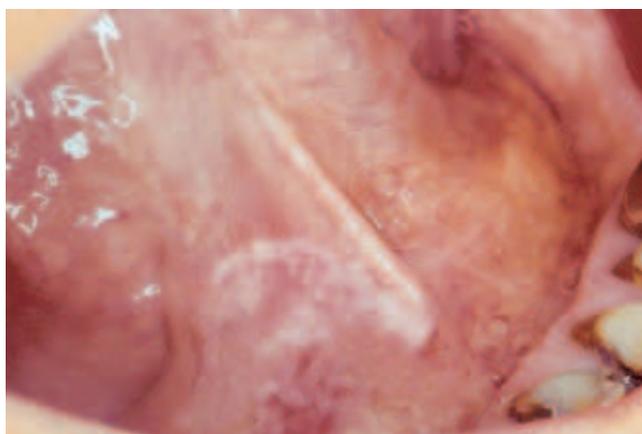
The buccal mucosa was the most commonly involved site (40.9%), followed by floor of the mouth (22.7%), corners of the mouth (18.1%), and the tongue (13.6%). As far as the clinical picture was concerned, leukoplakia simplex was the most frequent diagnosis (72.8%, Fig 1), followed by verrucous erosive leukoplakia (27.2%, Fig 5). Acanthosis, hyperorthokeratosis, and dysplasia were observed histopathologically in excised leukoplakia lesions (Figs 2 and 6). The wounds were left exposed to secondary epithelialization in the mouth (Figs 3 and 7). Macroscopic re-epithelization was assessed within 2 to 3.5 weeks (Figs 4 and 8).

Eight of the 14 subjects (57.1%) complained of minimal pain while eating or drinking products that were too hot/too cold or too spicy/too acidic 3 to 4 days following the procedure, depending on the size of surgical site. There were no other complaints of sensitivity or pain in 6 subjects at the 3-week follow-up examination. Clinical wound healing was complete in 3.5 to 5 weeks after treatment. In addition, no secondary infections occurred and there were no functional and/or esthetic problems during the follow-up period. Recurrence was seen in one patient who did not stop smoking. Biopsy was performed again of any new suspicious areas, but no dysplastic and/or atypical epithelial changes were observed.

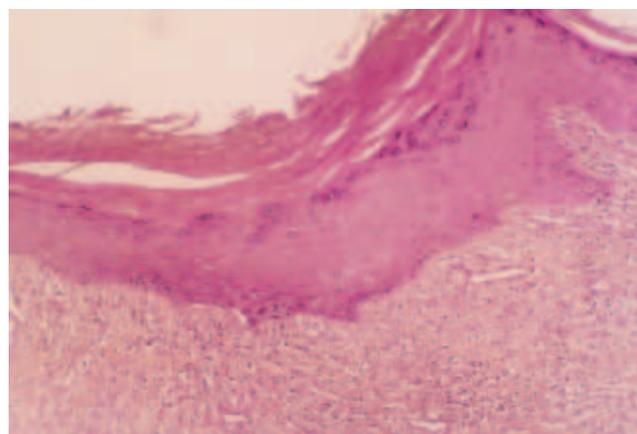
Periodic examinations have been continuing for 5 years. Figure 9 shows the full response of the lesion

**Table 1 Distribution of cases by age, gender, irritational factor, location, power, duration of epithelization and full keratinization, and recurrence during the 5-year follow-up**

Age/gender	Irritant	Location	Power(W)	Epithelization/ Clinical wound healing (weeks)	Recurrence (new leukoplakia patches)
44/M	Tobacco consumption	Right and left buccal mucosae	5	2.5/4	-
48/M	Tobacco consumption	Right and left buccal mucosae	5	2/3.5	-
49/M	Tobacco and alcohol consumption	Ventrum of the tongue	6	3/5	-
52/M	Tobacco consumption	Floor of the mouth	5	3/4.5	-
54/M	Tobacco and alcohol consumption	Floor of the mouth and lip	6	3/4.5	-
58/F	Tobacco consumption	Floor of the mouth	6	3/4.5	-
59/F	Tobacco consumption	Alveolar mucosa region 26	7	2.5/3.5	-
59/M	Tobacco and alcohol consumption	Right and left buccal mucosa	7	3/5	-
60/M	Tobacco and alcohol consumption	Corners of the mouth (right and left)	7	3/4.5	+
60/M	Tobacco and alcohol consumption	Dorsum of the tongue and ventral surface	6	3/4.5	-
60/F	Tobacco consumption	Right and left lip angles	6	3.5/5	-
62/F	Tobacco consumption	Right and left buccal mucosa	8	3/5	-
65/F	Tobacco consumption	Floor of the mouth	7	3/4	-
65/M	Tobacco consumption	Left lateral border of tongue and floor of the mouth	6	3/5	-



**Fig 1** Homogeneous, well-demarcated leukoplakia of the floor of the mouth in a 52-year-old male patient who smoked up to 25 cigarettes per day (Case 4).

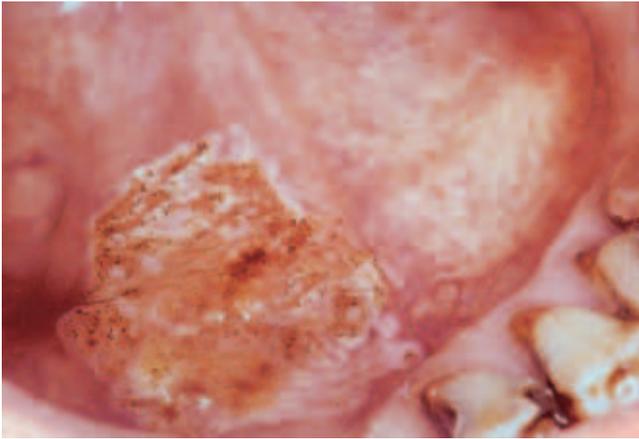


**Fig 2** Surface epithelium with atypical stratum spinosum layer. Heavy infiltration of lymphocytes and plasma cells in the subepithelial area. No tumor cells under the basement membrane (H&E stain, 250X).

without any sign of recurrence 5 years after the CO<sub>2</sub> laser ablation. Oral brush biopsies were obtained at each session throughout the follow-up period. Figure 10 shows the normal oral squamous epithelial cells of case 7.

## DISCUSSION

Leukoplakias may have similar clinical appearances, but have a considerable degree of microscopic heterogeneity. Because leukoplakias may range microscopically



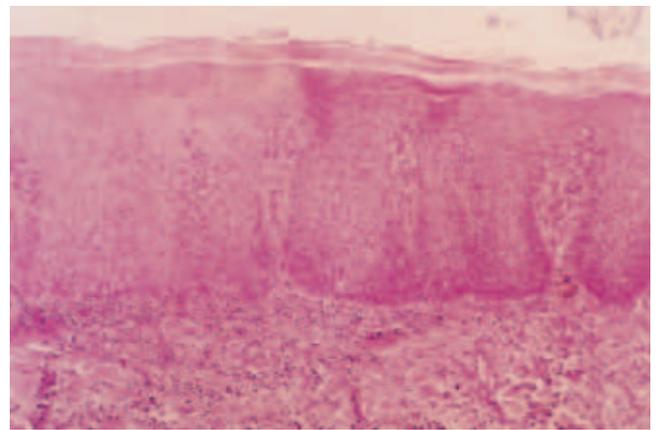
**Fig 3** Immediately after the CO<sub>2</sub> laser procedure.



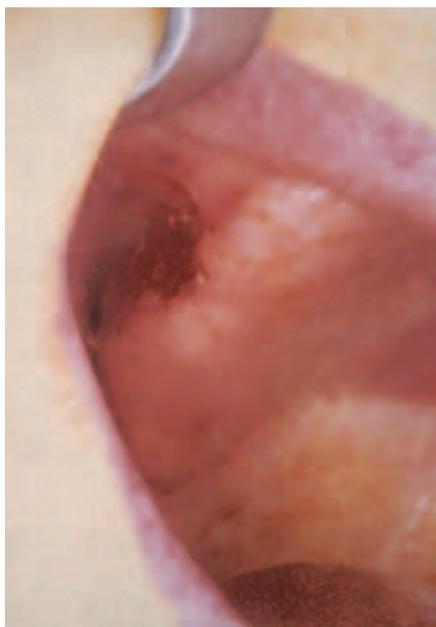
**Fig 4** The patient was re-examined and additional treatment was provided at a follow-up session. Wound healing was complete within 4.5 weeks.



**Fig 5** Clinical view of verrucous-erosive leukoplakia in a 59-year-old female patient (Case 7).

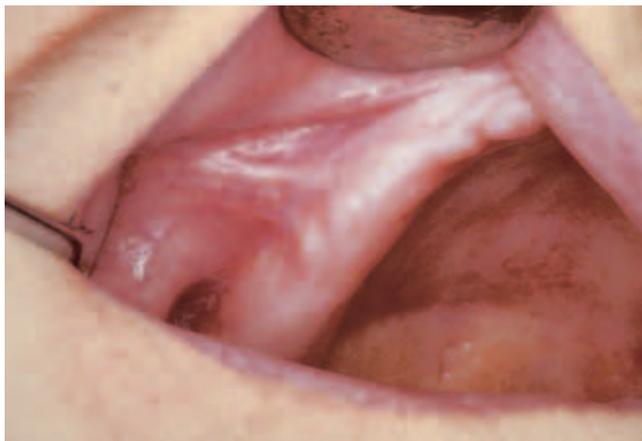


**Fig 6** Atypical epithelial cells in the papillary extension of the surface epithelium. Basement membrane is intact (H&E stain, 250X).

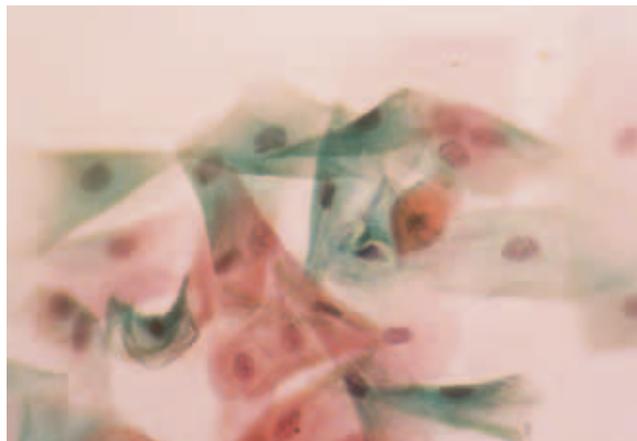


**Fig 8** Surgical site 2 weeks postoperatively.

**Fig 7 (left)** Immediate postoperative view of the lesion.



**Fig 9** Area after 5 years: treatment was successful, and leukoplakia did not recur.



**Fig 10** Routine oral smear shows normal surface epithelial cells on the clean background. Note uniform size, shape and position of nuclei with adequate surrounding cytoplasm (Papanicolaou stain, 400X) (Case 7).

from benign hyperkeratosis to invasive squamous cell carcinomas, a biopsy is mandatory to establish a definitive clinical diagnosis.<sup>1,3,6</sup>

The hemostatic property of lasers is of great value and provides the surgeon with better visibility of the area of interest. The importance of this property is evident in situations where strong hemorrhaging is likely (eg, leukoplakia of the tongue). Another aspect which should be emphasized is the better postoperative tissue healing and reduction of scar tissue formation due to decreased collateral tissue damage and fewer myofibroblastic cells in laser wounds.<sup>16-19</sup>

Horch et al,<sup>9</sup> Roodenburg et al,<sup>12</sup> Ishii et al,<sup>13</sup> Gaspar and Szabo,<sup>14</sup> and Chiesa et al<sup>15</sup> reported the use of the CO<sub>2</sub> laser in the treatment of leukoplakias, and concluded that the aforementioned technique has great advantages over conventional methods. Chiesa et al<sup>15</sup> documented the 3-year result of 145 oral leukoplakias surgically treated with CO<sub>2</sub> laser surgery (excision in 140 patients and vaporization in 5 patients) on an outpatient basis in an oncology institute. The rate of cancer and/or developing local relapses was 23% within one year. Horch et al<sup>9</sup> reported 22% recurrences in a 37-month follow-up. In contrast, after a 5-year follow-up, Roodenburg et al<sup>12</sup> found 90% of oral leukoplakias had healed and not recurred. In the present study, only 1 out of 22 leukoplakia lesions (1 of 14 patients) developed a slight recurrence in the right corner of the mouth.

Based on our observations and according to most authors, the surgical treatment of leukoplakias by CO<sub>2</sub>

laser is uneventful. CO<sub>2</sub> lasers have an affinity for wet tissue and are highly absorbed in oral mucosa, which is more than 90% water, although their penetration depth is only about 0.1 to 0.2 mm. Therefore, it allows precise removal in a virtually bloodless field; mucosa can be removed easily and thoroughly to a constant depth, while damage of the surrounding tissues is minimal. A further advantage was the versatile delivery system of the CO<sub>2</sub> laser beam.<sup>17-22</sup> In this way, even areas in the oral cavity that are difficult to reach with other systems can be treated. Power-to-tissue calibration was easy and could be conveniently performed at any time. There was no deep tissue damage and no wound contraction. Although the medication provided to the patients ensured comfort and swift recovery, 8 out of 14 patients complained of pain – depending on the size of the lesion – during the postoperative period.

The scalpel has distinct advantages over the laser: low cost and positive tactile feedback. Scalpel incisions heal more rapidly than those made by lasers. However, scalpel surgery usually causes complications in leukoplakia cases, particularly on the floor of the mouth, dorsum of the tongue, and the corners of the mouth. Thick scar tissue may be established after the operation. For large lesions, grafting procedures may be necessary after surgery.<sup>2,5</sup> Disadvantages of using laser on soft tissue lesions usually include a prolonged healing time due to the sealing of blood and lymphatic vessels. When compared to healing after scalpel surgery, restitutio ad integrum of the tissue takes at least 2 to 3 weeks.<sup>17</sup> The expense of laser systems and the rela-

tively longer rehabilitation period of treated areas seem the main disadvantages of the laser procedures.

Before considering the different lesions which can be successfully treated with laser, it is mandatory to remember that a blade biopsy must be taken of any kind of mucosal white lesion for histopathological examination prior to the operation. Therefore, CO<sub>2</sub> laser procedures should always be performed in conjunction with cytological and/or histological evaluation to determine the nature of the lesion. As with all pre-malignancies, operating protocol must be followed.<sup>1,5,6,13-15</sup>

In this study, the clinical effects of CO<sub>2</sub> laser treatment on the oral mucosa of subjects with leukoplakia were evaluated. One of the greatest advantages of CO<sub>2</sub> laser use was very high patient acceptance. All patients who had undergone surgery were advised that they should give up certain habits; nevertheless, 3 of the 14 patients did not follow this advice. It was also observed that stopping alcohol consumption was more difficult than stopping smoking.

## CONCLUSION

Concerning oral leukoplakia, CO<sub>2</sub> laser therapy can be considered as a first choice treatment, due to good surgical performance, a relatively painless postoperative period for many patients, and a highly predictable quality of tissue healing. It ensures effective management of the most confined and hard to reach areas (eg, dorsum of the tongue). Frequent clinical observation accompanied by photographic records and cytopathological or histological examination are recommended in white lesions. Moreover, the site of the leukoplakia is important in deciding on the surgery to be used. The dorsum of the tongue, the floor of the mouth, and the lips are sites with a high risk of cancer, while the buccal mucosa is the most frequently involved site but rarely shows cancer. It is vital to perform an immediate biopsy of any areas that are suspicious or that change in appearance, in view of the unpredictable behavior of dysplastic lesions.<sup>3,6,7,14-15</sup>

As for any procedure, advantages and limitations have to be carefully evaluated. Use of lasers in oral surgery should only be considered when the advantages outweigh the increased risk and cost of use.

## REFERENCES

1. Axell T, Pindborg JJ, Smith CJ et al. Oral white lesions with special reference to precancerous and tobacco related lesions: Conclusions of an international symposium held in Uppsala, Sweden, May 18-21 1994. *J Oral Pathol Med* 1996;25:49-54.
2. Reichart PA, Philipsen HA. Oral Pathology. In: Rateitschak KH, Wolf HF (eds). Stuttgart: Thieme, 2000:73,100,117.
3. Laskaris G. How to treat oral leukoplakia? *J Euro Academy Dermatol Venerol* 2000;14:446.
4. Ozbayrak S. Atlas of Oral Disease: Diagnosis, Differential Diagnosis and Treatment Approaches (in Turkish). Istanbul: Quintessence, 2003:100-110.
5. Regezi JA, Sciubba JJ, Jordan RCK. Oral pathology, clinical pathologic correlations, ed 4. Philadelphia: Saunders, 2003:86-90.
6. Silverman SJ, Gorsby M, Lozada F. Oral leukoplakia and malignant transformation: a follow up study of 257 patients. *Cancer* 1984;53:563-568.
7. Verdoft P, Holmstrup P, Hjorting-Hansen E, Pindborg JJ. Surgical treatment of premalignant lesions of the oral mucosa. *Int J Oral Maxillofac Surg* 1987;16:656-664.
8. Bekke JB, Baart JA. Six years' experience with cryosurgery in the oral cavity. *Int J Oral Surg* 1979;8:251-270.
9. Horch HH, Gerlach KL, Schaefer HE. CO<sub>2</sub> laser surgery of oral premalignant lesions. *Int J Oral Maxillofac Surg* 1986;15:19-24.
10. Chu FW, Silverman S Jr, Dedo HH. CO<sub>2</sub> laser treatment of oral leukoplakia. *Laryngoscope* 1988;98:125-130.
11. Flynn MB, White M, Tabah RJ. Use of carbon dioxide laser for treatment of premalignant lesions of the oral mucosa. *J Surg Oncol* 1988;37:232-234.
12. Roodenburg JL, Panders AK, Vermey A. Carbon dioxide laser surgery of oral leukoplakia. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 1991;71:670-674.
13. Ishii J, Fujita K, Komori T. Laser surgery as a treatment for oral leukoplakia. *Oral Oncol* 2003;9:759-769.
14. Gaspar L, Szabo G. The use of the CO<sub>2</sub> laser in the therapy of leukoplakia. *J Clin Laser Med Surg* 1989;7:27-29.
15. Chiesa F, Tradati N, Sala L, et al. Follow up oral leukoplakia after carbon dioxide laser surgery. *Arch Otolaryngol Head Neck Surg* 1990;116:177-180.
16. Arashiro DS, Rapley JW, Cobb CM, Killoy WJ. Histologic evaluation of porcine skin incisions produced by CO<sub>2</sub> laser, electro-surgery and scalpel. *Int J Perio Rest Dent* 1996;16:479-491.
17. Maiorana C. Lasers in the treatment of soft tissue lesions. *J Oral Laser Applic* 2003;3:7-14.
18. White JM, Chaundry SL. Nd:YAG and CO<sub>2</sub> laser therapy of oral mucosal lesions. *J Clin Laser Med Surg* 1998;16:299-304.
19. Pick RM, Pecaro BC. Use of the CO<sub>2</sub> laser in soft tissue dental surgery. *Laser Surg Med* 1987;7:207-213.
20. Gaspar L, Szabo G. Manifestation of the advantages and disadvantages of using the CO<sub>2</sub> laser in oral surgery. *J Clin Laser Med Surg* 1990;8:39-43.
21. Ozbayrak S, Dumlu A, Ercalick-Yalcinkaya S. Treatment of melanin pigmented gingiva and oral mucosa by CO<sub>2</sub> laser. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 2000;90:14-15.
22. Dumlu A, Ercalick-Yalcinkaya S, Ozbayrak S. CO<sub>2</sub> laser treatment of physiological melanin-pigmented oral tissues. *J Oral Laser Applic* 2003;3:211-217.

**Contact address:** Dr. Sebnem Ercalick Yalcinkaya, Marmara University Faculty of Dentistry, Department of Oral Diagnosis and Radiology, Büyükciftlik sk. No: 6 Nisantasi 80200, Istanbul, Turkey. Tel: +90-212-231-9120, Fax: +90-212-231-2987. e-mail: sebnemer@rocketmail.com