Journal of Cranio-Maxillo-Facial Surgery 43 (2015) 677–681

Contents lists available at ScienceDirect

Journal of Cranio-Maxillo-Facial Surgery

journal homepage: www.jcmfs.com

The treatment of oral leukoplakia with the CO_2 laser: A retrospective study of 65 patients

Alfonso Mogedas-Vegara [a, *], Juan-Antonio Hueto-Madrid [a], Eduardo Chimenos-Küstner [b], Coro Bescós-Atín [a]

[a] Oral and Maxillofacial Department, Vall D'Hebron University Hospital, Universidad Autónoma de Barcelona, Passeig de la Vall D'Hebron 119-129, Barcelona 08035, Spain
[b] Oral Medicine, Oral Pathology, Oral Surgery Department, Universidad de Barcelona, Feixa Llarga s/n, L'Hospitalet Ll., Barcelona 08907, Spain

ARTICLE INFO

Article history:
Paper received 18 June 2014
Accepted 18 March 2015
Available online 26 March 2015

Keywords:
Oral leukoplakia
CO_2 laser
Recurrence
Malignant transformation
Potentially malignant oral disorder
Oral dysplasia

ABSTRACT

The use of CO_2 laser has become a routine procedure for the treatment of oral leukoplakia. In this retrospective study, we evaluated 65 patients with oral leukoplakia treated with CO_2 laser vaporization. The main location was the tongue (n = 21/65, 32.3%). The initial biopsy showed mild/moderate dysplasia in almost half the patients (n = 29, 44.6%) and hyperplasia without dysplasia in around a third of the patients (n = 21, 32.3%). The recurrence and malignant transformation rates were 33.8% (n = 22) and 15.4% (n = 10), respectively. The follow-up mean (standard deviation) was 15.0 (10.6) months. The procedure-related complications rate was 7.7% (n = 5). The Kaplan–Meier curves for time to recurrence showed differences only for gingiva lesions compared to tongue lesions (log rank, p = 0.032). Malignant leukoplakia transformation is independent of treatment, although it seems advisable to treat leukoplakia with or without dysplasia.

1. Introduction

The World Health Organization (WHO) first defined oral leukoplakia as a white patch or plaque that could not be characterized clinically or pathologically as any other disease (Axell et al., 1996). At a workshop coordinated by the WHO in 2005, "potentially malignant disorder" was the preferred terms, with the working group agreeing that the term leukoplakia should be used to recognize "white plaques of questionable risk having excluded (other) known diseases or disorders that carry no increased risk for cancer" (Warnakulasuriya et al., 2007). Prevalence of oral leukoplakia is reported to be approximately 2% (Petti, 2003; Brouns et al., 2013a, 2013b) and the annual malignant transformation rate is estimated to be between 0.13% and 17.5% (Deppe et al., 2012; Kumar et al., 2013; Brouns et al., 2014). Leukoplakia is considered to be the most common premalignant lesion of the oral cavity; its occurrence is related to smoking, with alcohol as an independent factor. The role played by human papilloma virus is currently unknown (Van der Waal, 2009). Risk factors associated with malignant leukoplakia transformation are: female gender, longer duration, non-smokers, location on the tongue, size >200 mm^2, nonhomogeneous type and presence of *Candida albicans*, or epithelial dysplasia (Van der Waal, 2009, Ho et al., 2013). Head and neck cancers are the sixth most common cancer worldwide and are considered an important public health problem because of the poor prognosis and associated high morbidity and mortality (Jerjes et al., 2011).

Incisional biopsy and histopathological examination are the gold standard in diagnosis. Early detection of oral lesions increases survival rates; hence, early and minimally invasive treatment would be indicated for those patients who would be expected to have low recurrence rates (Deppe et al., 2012; Brouns et al., 2013a; Kumar et al., 2013). Several treatments have been suggested in the literature, including surgery, electrosurgery, cryosurgery, topical agents (bleomycin, vitamin A), systemic agents (β-carotene, lycopene, retinoids), CO_2 laser and photodynamic treatment, although surgery and CO_2 laser are most frequently used. There is still no evidence that treatment prevents malignant transformation, although it seems advisable to treat oral leukoplakia with or without dysplasia (Horch et al., 1986; Chandu and Smith, 2005; Van

* Corresponding author. Carrer Enric Granados 67,3°,1, 08008 Barcelona, Spain. Tel.:+34 636578302.
E-mail address: Alfonso.mogedas@icloud.com (A. Mogedas-Vegara).

http://dx.doi.org/10.1016/j.jcms.2015.03.011
1010-5182/

der Waal, 2009; Santos et al., 2010; Yang et al., 2011; Song and Franco, 2011; Brouns et al., 2014).

New technologies and improvements in oral and maxillofacial surgery and especially in laser surgery prove less invasive and more comfortable for patients. The use of CO_2 laser is becoming increasingly common in the treatment of oral leukoplakia and malignant tumours, with outcomes, advantages and disadvantages fully reported in the literature (Chandu and Smith, 2005; Escribano-Bermejos and Bascones-Martínez, 2009; Yang et al., 2011; Deppe et al., 2012; Goodson et al., 2012). CO_2 laser can be used for both excision and vaporization. For vaporization, preferred for large lesions, a prior biopsy is necessary (Chandu and Smith, 2005; Santos et al., 2010; Deppe et al., 2012; Brouns et al., 2013a, 2014). Vaporization has also been used to resect small (T1/T2) oral squamous cell carcinoma (OSCC), with results comparable to those of surgery (Jerjes et al., 2011).

We retrospectively reviewed the results for a sample of patients with oral leukoplakia treated with CO_2 laser. Our main objective was to evaluate treatment results, and our secondary objectives were to determine the recurrence and malignant transformation rates, to quantify complications associated with the procedure, and to suggest a follow-up protocol.

2. Material and methods

A total of 65 patients were treated with CO_2 laser vaporization between January 2010 and April 2013. Medical records were reviewed to evaluate demographic data, history of OSCC, location of the lesion, histological malignancy grade, complications, recurrences, and malignant transformation.

A histopathological diagnosis of leukoplakia was obtained prior to surgery on the basis of an incisional biopsy. All surgical procedures were performed under local anesthesia via local tissue infiltration with articaine hydrochloride (72.0 mg) and epinephrine (0.018 mg). A Lumenis CO_2 laser (10.6-μm wavelength) set up in superpulse focused mode was used for vaporization (15 W). The mucosa–handpiece distance was 15–20 mm, handpiece focus length was 125 mm, laser exposure was 20 s, spot diameter was 0.3 mm, and fluence energy was 4,244 J/cm^2. Depending on the location of the lesion, buccal mucosa, lip, or tongue were separated using gauze. The laser was tested on a moist gauze prior to each surgery, and the mandatory special mask and glasses were worn. A high-potency vacuum device was used to aspirate the laser plume. Clinical pictures of the oral leukoplakia were taken in the operation room and during follow-up. Prescribed for postoperative care were 0.12% chlorhexidine gel and 600 mg of ibuprofen every 8 h. Follow-up examinations were performed according to our protocol on day 7 after surgery, every 3 months in the first year, every 6 months in the second year, and annually thereafter.

2.1. Statistical analysis

Demographic and clinical variables were analyzed descriptively, and categorical variables were reported as frequencies and percentages. The Shapiro–Wilks statistic was used to test the distribution of continuous variables, described as mean (standard deviation) if they followed a normal distribution or as median (interquartile range) otherwise. Kaplan–Meier curves with log-rank tests were used to assess time to recurrence and malignant transformation according to the different clinical characteristics of interest. Univariate Cox regression was used to identify risk factors for recurrence and malignant transformation, calculating the hazard ratio (HR) and establishing a 95% confidence interval (95% CI). A p value of less than 0.05 in these tests was considered to indicate statistical significance. SPSS 18.0 for Windows (SPSS Inc, Chicago, IL, USA) was used for all statistical analyses.

3. Results

The study cohort consisted of 65 patients who underwent vaporization at our center between January 2010 and April 2013. The median follow-up was 15.0 (0.3–38.7) months. Demographic and clinical characteristics of the patients are summarized in Table 1. Just under half the patients were male (n = 32, 49.2%), patient mean age at surgery was 66.2 (13.1) years, and 15 patients (23.1%) had a history of OSCC. Primary sites were mainly identified in the tongue (n = 21, 32.3%) and the gingiva (n = 19, 29.2%). The initial biopsy showed mild/moderate dysplasia in almost half the patients (n = 29, 44.6%) and hyperplasia without dysplasia in around a third of patients (n = 21, 32.3%). Half the gingiva lesions presented no dysplasia (n = 10/19, 52.6%). The procedure-related complications rate was 7.7% (n = 5), with all complications associated with postoperative pain that required nonsteroidal anti-inflammatory drug treatment.

During follow-up, 22 patients (33.8%) had a recurrence, representing an annual rate of 35.3% (95% CI = 22.1–53.4). The main characteristics of this group and potential risk factors for recurrence are summarized in Table 2. No differences were observed by gender, smoking and alcohol consumption, number of lesions, histological grade, or previous history of OSCC. Lesion location in the gingiva as opposed to the tongue was found to be a risk factor. Kaplan–Meier curves for time to recurrence (Fig. 1) showed differences only for lesion location in the gingiva compared to the tongue (log rank, p = 0.032).

During follow-up, 10 patients (15.4%) presented with malignant transformation, representing an annual rate of 12.3% (95% CI = 6.0–22.7). The main characteristics of this group and potential risk factors for malignant transformation are summarized in Table 3. No differences were observed by gender, smoking and alcohol consumption, number of lesions, or histological grade. Lesion location in the gingiva as opposed to the tongue a history of OSCC showed a tendency to be risk factors for malignant transformation.

Table 1
Demographic and clinical data.

	Total n (%) (n = 65)	Recurrence n (%) (n = 22)	Malignant transformation n (%) (n = 10)
Mean age (y)	66.2	66.6	66.6
Male	32 (49.2)	9 (40.9)	5 (50)
Smokers	36 (55.4)	13 (59.1)	4 (40)
Alcohol consumers	25 (38.5)	9 (40.9)	5 (50)
Leukoplakia location			
Tongue	21 (32.3)	7 (31.8)	4 (40)
Gingiva	19 (29.2)	10 (45.5)	3 (30)
Lip	5 (7.7)	2 (9.1)	–
Buccal mucosa	10 (15.4)	1 (4.5)	2 (20)
Floor of mouth	4 (6.2)	1 (4.5)	1 (10)
Retromolar trigone	3 (4.6)	1 (4.5)	–
Palate	3 (4.6)	0	–
Multiple sites	15 (23.1)	7 (31.8)	2 (20)
Dysplasia grade			
0	21 (32.3)	7 (31.8)	2 (20)
1	29 (44.6)	12 (54.5)	4 (40)
2	8 (12.3)	2 (9.1)	2 (20)
3	7 (10.8)	1 (4.5)	2 (20)
OSCC history	15 (23.1)	7 (31.8)	6 (60)
Complications	5 (7.7)	3 (13.6)	2 (20)
Re-vaporization	20 (30.8)	20 (90.9)	–
Malignant transformation	10 (15.4)	5 (22.7)	–