Journal of Cranio-Maxillo-Facial Surgery 43 (2015) 763–768

Contents lists available at ScienceDirect

Journal of Cranio-Maxillo-Facial Surgery

journal homepage: www.jcmfs.com

Laser evaporation versus laser excision of oral leukoplakia: A retrospective study with long-term follow-up

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ARTICLE INFO

Article history:
Paper received 13 January 2015
Accepted 8 April 2015
Available online 17 April 2015

Keywords:
Laser surgery
Oral leukoplakia
Laser excision
Laser evaporation
Nd:YAG laser
CO_2 laser

ABSTRACT

Objectives: The study makes a comparison between two surgical approaches for the treatment of oral leukoplakia (OL) in terms of recurrence in a well-defined cohort of patients with a long-term follow-up period.
Methods: The cohort consisted of 77 OL patients divided into 2 groups. Group 1: 47 patients treated with laser evaporation using a Nd:YAG laser. Group 2: 30 patients treated with a CO_2 laser for excision. Clinical and histological examinations were performed for the diagnosis of OL before treatment. We included OLs with or without dysplasia. The mean follow-up period was 60 ± 32.49 months.
Results: Of the 77 patients, 22 (28.5%) showed recurrence during the follow-up period. No significant difference was found between the two treatments ($\chi^2 = 2.6$; $p = 0.2$). However, CO_2 laser excision resulted in better results than the Nd:YAG laser evaporation, considering the non-homogeneous OLs ($\chi^2 = 3.9$; $p = 0.04$) and OLs with mild dysplasia ($\chi^2 = 4.6$; $p = 0.03$).
Discussion: The study makes a comparison between our results and articles from the literature, and suggests when each of the two surgical approaches is most appropriate.

1. Introduction

Oral squamous cell carcinoma (OSCC) is the most common tumour of the oral cavity with 5-year and 22-year survival rates of 30–45% and 6.3%, respectively, while locoregional recurrence after treatment occurs in almost 30% of cases (Lopez-Cedrun and Andres de Liano, 2015; Kreppel et al., 2013). Oral leukoplakia (OL) is considered a premalignant oral lesion, and its diagnosis is essentially made by excluding other known diseases. The prevalence of OL worldwide is ~2% (Petti, 2003), and it is more frequent in smokers than non-smokers. Its diagnosis is made by clinical features, and a biopsy is mandatory to exclude other diseases. OL is a white plaque, and is divided into homogeneous and non-homogeneous types: the homogeneous type is a white plaque that is flat, thin, and uniform, whereas the non-homogeneous type can be irregularly flat, nodular, verrucous, and with a white and red colouration (van der Waal, 2010). With respect to non-homogeneous OL, proliferative verrucous leukoplakia (PVL) can involve any site in the oral cavity and has a high risk of malignant transformation (van der Waal and Reichart, 2008). A histological examination must be performed to exclude other diseases, and in particular, to determine the presence of dysplasia (mild, moderate, or severe; low-grade intraepithelial lesion or high-grade intraepithelial lesion, according to the 2014 Ljubljana classification). Malignant transformation ranged from 0.13% to 17.55% (Lee et al., 2006; Reibel, 2003). Thus, not all OL cases transform into OSCC. A high risk of malignant transformation is correlated with the degree of histological dysplasia.

Treatment modalities range from cessation of smoking to medication with retinoids, cryosurgery, or laser surgery. Laser

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http://dx.doi.org/10.1016/j.jcms.2015.04.009
1010-5182/

surgery was first performed in 1978 (Ben-Bassat et al., 1978). It presents some advantages, such as total removal of the lesion, minimal damage to surrounding tissues, and reduction of post-operative pain and oedema (van der Hem et al., 2005). Healing is typically very good because of the limited contraction of the tissues and minimal oral dysfunction (Ishii et al., 2003). CO_2 and Nd:YAG lasers are mainly used to treat OL in two different modalities: evaporation and excision. Evaporation induces limited post-operative discomfort, and can be performed in different stages, especially in patients with wide lesions or multiple lesions. The main disadvantage of the evaporation technique, with respect to excision, is the impossibility of examining the whole lesion histologically. In addition, excision can lead to functional problems with very large lesions.

The present study describes, for the first time, a comparison between the two different surgical approaches for the treatment of OLs: Nd:YAG laser evaporation versus CO_2 laser excision. The long-term follow-up and the two different cohorts of patients validate this retrospective study. The objective was to assess whether there were significant differences in terms of recurrence between the two surgical treatments.

2. Materials and methods

From 2004 to 2013, 77 OL cases were diagnosed at the Department of Oral Sciences of the University of Bologna, after which they were treated at the Maxillo-Facial Unit of the S. Orsola Hospital, Bologna, Italy.

2.1. Inclusion and exclusion criteria

Only patients referred to the Department of Oral Sciences, University of Bologna, with a diagnosis of OL were included. The inclusion criteria were OLs with or without dysplasia and clear surgical margins on histological examination. Patients with pre-existing OSCC, OLs with severe dysplasia (high-grade intra-epithelial lesion, according to the 2014 Ljubljana classification), and patients with other white lesions not identifiable as OL were excluded. In addition, surgical specimens with positive dysplastic margins and OSCC found in the first surgical specimen were excluded.

2.2. Patient management

All of the patients underwent histological examination for diagnosis. Specimens were taken with a biopsy punch to a depth of at least 5 mm, and a 3–5 mm margin of clinically normal mucosa was also included. All of the tissues were fixed in 10% formalin and paraffin wax-embedded by routine procedures. Serial sections were cut from each block, and stained with haematoxylin and eosin for histological evaluation. Histological examinations and immunohistochemical staining were performed blindly at the Section of Anatomic Pathology of the Department of Hematology and Oncology, Bologna University, at Bellaria Hospital. All of the cases were examined by the same pathologist (MPF). Histological diagnoses were performed according to the WHO criteria.

Table 1
Age and sex distribution of patients treated with laser evaporation (Group 1) and laser excision (Group 2) respectively.

		Number	Age (year)	Mean (year)
Group 1	Men	19	34–78	55
	Women	28	42–80	60
	Total	*47*	*34–80*	*58*
Group 2	Men	19	34–79	65
	Women	11	26–80	57
	Total	*30*	*26–80*	*62*

Table 2
The sites of all the lesions.

Site	Number	Percentage
Tongue	18	23%
Floor of the mouth	5	6.5%
Hard palate	8	10%
Buccal mucosa	25	32.5%
Upper or lower gingiva	21	28%
Total	77	100%

Age, gender distribution, site of the lesions, and grade of dysplasia at the biopsy are shown in Tables 1–3. The sites of OL were the tongue, floor of the mouth, hard palate, buccal mucosa, and upper and lower gingiva. Treatment consisted of the surgical excision of the OLs. Group 1 consisted of 47 OLs treated with laser evaporation with a Nd:YAG laser; Group 2 consisted of 30 OLs treated with CO_2 laser excision. All of the treatments were performed under local anaesthesia, except some larger lesions where excision was performed under general anaesthesia. Laser treatment was performed at the Laser Centre of S. Orsola Hospital (Bologna, Italy) by the same surgeon, using a 1064 nm Nd:YAG laser (Model 6000, Laser Sonics, Cooper Laser Sonics) with a laser spot of 600 μm. The laser beam was set at 9 W for the lip, tongue, and marginal gingiva, and at 12 W for the remaining areas, and was administered in pulsed mode (0.3 s followed by a 0.1 s pause). Power density ranged from 3200 W/cm^2 to 4200 W/cm^2. The total energy irradiated and the time needed for complete ablation depended on the extent of the treated areas, varying from 3 to 10 min with a total maximum power of 300 J (Montebugnoli et al., 2012). A different laser was used for the excision: a CO_2 laser (Deka Smart Office + LCD) with a laser spot of 200 μm and a wavelength of 10.6 μm. The laser beam was set at 8–15 W, and used in pulse mode (0.5 s followed by a pause of 0.1 s) with a 20 Hz frequency. The time of excision depended on the extent of the lesion, ranging from 10 to 15 min. The laser was used in focused mode to obtain a precise cut at a distance of 1.5 cm from the oral mucosa. The excision of the lesions included 3–5 mm of normal mucosa surrounding the lesion. The depth of excision involved the mucosal and submucosal layers.

The analysis endpoint was considered the appearance of recurrence. Recurrence was considered to be a leukoplakia arising in the same site as the first, within the borders of the treated area (Ben-Bassat et al., 1978). To evaluate the recurrence rate, we only included patients with a minimum follow-up of 6 months. Follow-up visits were scheduled 1 week after the treatment, and until healing was achieved with intervals of 3, 6, or 12 months,

Table 3
The grade of dysplasia (and Ljubljana 2014 classification) at the biopsy of patients treated with laser evaporation (Group 1) and laser excision (Group 2) respectively.

	Dysplasia	Lujbljana 2014 classification	Number	Percentage
Group 1	No dysplasia	Low grade intraepithelial lesion	35	75%
	Mild	Low grade intraepithelial lesion	11	23%
	Moderate	High grade intraepithelial lesion	1	2%
	Severe	High grade intraepithelial lesion	0	0%
	Total		47	100%
Group 2	No dysplasia	Low grade intraepithelial lesion	18	60%
	Mild	Low grade intraepithelial lesion	5	17%
	Moderate	High grade intraepithelial lesion	7	23%
	Severe	High grade intraepithelial lesion	0	0%
	Total		30	100%