



Oral leukoplakia treatment with the carbon dioxide laser: A systematic review of the literature



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ABSTRACT

We conducted a systematic review of the literature to evaluate treatment of oral leukoplakia with the carbon dioxide (CO₂) laser.

A comprehensive search of studies published between 1981 and 2015 and listed in the PubMed (National Library of Medicine, NCBI) database yielded 378 articles which were screened in detail. Relevant studies were selected according to predetermined inclusion and exclusion criteria. A total of 33 articles met the final inclusion criteria and were analysed in detail in accordance with the PRISMA-P statement. These full-text papers were classified as synopses (n = 7), recurrence and malignant transformation studies (n = 17), comparative studies between CO₂ laser and cold knife surgery (n = 3) and studies evaluating the efficacy of CO₂, Nd:YAG and KTP lasers.

According to the literature the CO₂ laser is the workhorse of oral leukoplakia treatment due to its effectiveness and low associated morbidity. However, randomized clinical trials are needed to compare CO₂ laser with other lasers. The results of our systematic review showed that there is no consensus regarding the factors involved in higher recurrence and malignization rates, so further studies are needed.

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1. Introduction

Oral leukoplakia (OL) is the most common potentially malignant lesion of the oral cavity, leading, in some cases, to oral squamous cell carcinoma (OSCC). The annual rate of malignant transformation of OL into OSCC is approximately 1%–2% (Van der Waal, 2009).

Several treatment options have been used for OL, but, according to the literature, cold knife surgery and carbon dioxide (CO₂) laser surgery seem to offer better outcomes than topical or systemic medication in terms of recurrence and malignant transformation. Although there is no evidence that treatment prevents malignant transformation, it is recommended to treat OL with or without dysplasia (Horch et al., 1986; Chandu et al., 2005; Brouns et al., 2014a).

The CO₂ laser was invented in 1963 by Patel (1964), but Ben-Bassat et al. (1987) were the first to describe its use for intraoral treatment. Since then many studies have endorsed the advantages and effectiveness of the CO₂ laser as treatment not only for OL, but also for other oral and maxillofacial lesions and head and neck lesions (Chandu et al., 2005; Yang et al., 2011; Deppe et al., 2012).

The aim of the present review article was to systematically evaluate the effectiveness of CO₂ laser treatments on OL lesions.

2. Material and methods

2.1. Search strategy

A MEDLINE (PubMed) search was conducted, with studies published from 1981 to 2015 included in the systematic review (SR). The SR was updated on 16th June 2015 and conducted in accordance with the Preferred Reporting Items for Systematic

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Reviews and Meta-Analysis protocols (PRISMA-P 2015) (Moher et al., 2015). All eligible articles were manually checked for additional references.

2.2. Search terms

A combination of the following keywords was used: oral leukoplakia, vaporization, CO₂ laser, carbon dioxide laser, laser surgery, epithelial dysplasia, malignant transformation, and recurrence.

2.3. Article selection

To control for selection bias, two independent reviewers (AMV and JAHM) evaluated the titles and abstracts of retrieved articles. If it was not clear from the title and abstract whether an article met the inclusion criteria, the full text was reviewed. Expert opinions were excluded. When duplicate reports of the same study were identified, only the most recent was included. Full-text articles were then evaluated and differences between both reviewers were solved by discussion until consensus was reached.

2.4. Inclusion criteria

The inclusion criteria for the studies were as follows: studies reporting clinical series of patients with OL treated with the CO₂ laser, studies reporting clinical series of patients with OL treated with CO₂ laser compared to other surgical techniques and, finally, articles dealing with general aspects of OL treatment with the CO₂ laser.

2.5. Exclusion criteria

The exclusion criteria were as follows: duplicated studies, animal studies, experimental laboratory studies, cohort studies with less than 12 months follow-up, articles reporting leukoplakia in locations other than oral, articles published in languages other than English, French, German, Italian and Spanish and, finally, letters, editorials and abstracts.

2.6. Data collection and analysis

The following information was collected, when possible, from the selected studies: first author, year, country, number of patients treated with CO₂ laser, number of different OL lesions treated in each study, the most frequent locations for OL, recurrence rate, malignant transformation rate, type of CO₂ laser used and the complications rate. Whenever possible, data on factors affecting recurrence and malignant transformation were also collected.

3. Results

The initial MEDLINE search retrieved 378 articles. For multiple publications regarding the same group of patients, only the most recent study was included. Initial analysis of titles and abstracts eliminated 314 articles, leaving 64 articles whose full text was examined. A total of 33 studies met the inclusion criteria and so were included in the final review. Studies were classified into 4 groups (Table 1).

3.1. Synopsis articles

Seven of the articles (21.21%) were synopses. Huang et al. (2015) retrospectively evaluated the safety and advantages of using CO₂ laser in the treatment of oral mucosal lesions including vascular

Table 1

Classification of analysed oral leukoplakia articles (n = 33). 1. Synopses. 2. Studies of recurrence and malignant transformation. 3. Comparative studies between CO₂ laser and cold knife. 4. Studies evaluating the efficacy of CO₂, Nd:YAG and KTP laser.

	Number of articles	Percentage
1. Synopses	7	21.21%
2. Studies of recurrence and malignant transformation	17	51.51%
3. Comparative studies between CO ₂ laser and cold knife	3	9.9%
4. Studies evaluating the efficacy of CO ₂ , Nd:YAG and KTP laser	6	18.18%

malformations, OL and verrucous nevus in a group of 73 patients, comparing their results with a control group of 20 patients treated with the traditional scalpel. They found statistically significant ($p < .05$) better outcomes in terms of shorter operative time and less bleeding in the patients treated with the CO₂ laser. Deppe et al. (2012) prospectively evaluated recurrence rates resulting from different methods of CO₂ laser vaporization (defocused continuous wave, superpulsed mode plus scanner and continuous wave plus scanner), concluding that recurrence rates were lower to a statistically significant degree for the defocused continuous wave technique followed by the continuous wave scanner and the superpulsed plus scanner mode, in that order. Metzler (2007) reviewed the literature on surgical management of oral mucosal dysplasia, describing the technique, advantages and disadvantages of CO₂ laser for OL treatment. Colella et al. (1995) reviewing the literature on different methods of OL treatment, particularly focussing on CO₂ laser, traditional surgery and natural or synthetic retinoids. Deymes (1981) reported experiences with CO₂ laser for OL treatment and also for other intraoral benign neoplasms. Roodenburg and Horch (1993) reviewed indications for CO₂ laser in oral and maxillofacial surgery, describing advantages over other methods and concluding it to be the treatment of choice for OL. Bornstein et al. (2003) reviewed and discussed recurrence and malignant transformation rates for studies of OL treated with the CO₂ laser from 1985 to 2000, focussing especially on complications and wound healing.

3.2. Studies of recurrence and malignant transformation

Seventeen papers (51.51%) were classified as studies focussing on recurrence and malignant transformation of OL in patients treated with the CO₂ laser. These studies are summarized in Table 2 (Frame, 1985; Horch et al., 1986; Chu et al., 1988; Roodenburg et al., 1991; Chiesa et al., 1993; Huerta et al., 1999; Gooris et al., 1999; Dunsche et al., 2000; Thomson et al., 2002; Van der Hem et al., 2005; Chandu et al., 2005; Yang et al., 2011; Jerjes et al., 2012; Brouns et al., 2013, 2014; Pedrosa et al., 2015; Mogedas-Vegara et al., 2015).

All the articles were retrospective, with patients treated for different OL locations, except for one article that focused exclusively on leukoplakia of the lower lip (Gooris et al., 1999). Some studies aimed to identify the factors (epidemiological, etiological, clinical and histopathological) affecting recurrence and possibly predicting malignant transformation (Table 3).

3.3. Comparative studies between CO₂ laser and cold knife surgery

Three papers (9.9%) prospectively compared excision of OL by CO₂ laser versus traditional scalpel (Che et al., 2012; López-Jornet et al., 2013; Tambuwala et al., 2014). Table 4 summarizes these studies and the parameters used to compare the two methods ($p > .05$ was considered to be statistically significant).

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