REVIEW Lib Oncol. 2016;44(2–3):37–43

COMPARISON OF DIFFERENT LASERS IN THE TREATMENT OF PRECANCEROUS LESIONS OF THE ORAL CAVITY

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Summary

Various treatment procedures for precancerous lesions in the oral cavity have been reported: excision surgery, electrocoagulation, cryosurgery, laser surgery, the local use of corticoids and administration of vitamin A. The main objective in the treatment of precancerous lesions of the oral cavity is to remove potentially neoplastic cells due to the possibility of recurrence and/or malignant transformation from those cells. Lasers are widely accepted and used in medicine and dentistry due to their beneficial effects: coagulation properties (less perioperative and postoperative bleeding), and less postoperative pain and oedema. Furthermore, laser therapy results in good and fast healing process, a low level of patient's discomfort during and after surgical intervention, as well as rapid disappearance of postsurgical symptoms. Pubmed was searched in order to find out published papers in the last 20 years (1996-2016) regarding the usage of various lasers in the treatment of precancerous lesions of the oral cavity. Using the terms "laser" and "oral precancerous lesion" 27 articles were found in the searched period. Since the oral leukoplakia is the most precancerous condition in the oral cavity, next search was based on the terms "laser" and "oral leukoplakia" when 122 articles were found. Review articles and clinical trials written on the English language were included in presented systematic review.

KEY WORDS: *precancerous lesion, leukoplakia, erythroplakia, oral lichen planus, laser, surgery*

USPOREDBA RAZLIČITIH LASERA U LIJEČENJU PREKANCEROZA U ORALNOJ ŠUPLJINI

Sažetak

U liječenju prekanceroza u oralnoj šupljini, koriste se standardne kirurške tehnike, laserska kirurgija, kriokirurgija, elektrokoagulacija, lokalna uporaba kortikosteroida i vitamina A. Tim postupcima uklanja se prekancerozno tkivno, sprječava maligna transformacija i metastaziranje. Laser je prihvaćen u medicini zbog manjeg operacijskog i poslijeoperacijskog krvarenja, boli, edema i bržeg cijeljenja rane. Pretražena je baze podataka PubMed - NCBI o uporabi lasera za liječenje oralnih prekanceroza u razdoblju od 20 godina (1996. do 2016.) Pod ključnim riječima "laser! i "oral precancerous lesion", nađeno je 27 članaka. Leukoplakija je najčešća prekanceroza u ustima, pa je pod "laser" i "oral leucoplakia" nađeno 122 članka. Slijedi osvrt na te radove.

KLJUČNE RIJEČI: *prekanceroze, leukoplakija, eritroplakija, ustni lichen planus, laser, kirurgija*

INTRODUCTION

Lasers are widely accepted and used in medicine and dentistry due to their beneficial effects such as: coagulation properties (less perioperative and postoperative bleeding), and less postoperative pain and oedema. Furthermore, laser therapy results in good and fast healing process, a low

level of patient's discomfort during and after surgical intervention, as well as rapid disappearance of postsurgical symptoms (1). The main objective in the treatment of precancerous lesions of the oral cavity is to remove potentially neoplastic cells due to the possibility of recurrence and/or malignant transformation from those cells (2).

Laser surgery has many advantages for both the surgeon and patient. It can control hemorrhaging while the surgeon has excellent visibility during operation and enables shortening of the operative time. Patients do not require a special method to stop bleeding after surgery. In addition, there is minimal damage to adjacent tissue, thus reducing acute inflammatory reactions and postoperative pain, swelling, oedema or infections. Sealing of blood and lymphatic vessels diminishes the risk of disseminating neoplastic cells int he treatment of malignant lesions, and sealing oft he nerve endings reduces postoperative pain (3). Laser surgery results in excellent healing process because of the limited scarring and contraction, and there is satisfactory mobility of the soft tissues. However, laser surgery has some disadvantages. The major is that the biopsy should be obtained using other methods, preoperatively or at the time of laser treatment. Epithelial regeneration after laser surgery is delayed, and wound healing process takes longer to re-epithelialize when compared to conventional surgery. The last disadvantage is safety precautions, namely, the use of eye-glasses is required to protect both the patient and the medical staff (4).

However, some authors speculate that temperature-induced injuries due to laser light application and questionable possibility of post-operative histopathological evaluation of the sampled tissue might be a drawback in laser use. Azavedo et al. (5) reported that different lasers using different parameters (Er:YAG at 2W with and without air/water spray and at 4W with and without air/water spray; CO_2 at 3.5W and 7W in pulsed mode and at 7W in continuous mode; the diode laser at 3.5W and boost 3.5W in pulsed mode; Nd:YAG at 6W, 40Hz) can be used in soft oral tissues biopsies as they are capable of providing a correct histopathological analysis. This study was performed on pork mucosa.

The main asset of the CO_2 laser comparing to Er:YAG laser is an effective coagulation while thermal injury to the tissues is its limitation, especially with multiple passage of the beam and too high power applied. Er:YAG laser application does not exclude histopathological examination of the removed lesion tissue which is its advantage over CO_2 laser. Still, insufficient coagulation is a limitation of its use in the case of richly vascularized lesions (6). Kharadi et al. (7) applied 940 nm diode laser in ten patients with oral leukoplakia and reported perfect healing process and mild pain intensity.

Some results indicate that for CO_2 laser treatment of premalignant lesions of the oral mucosa, the best results can be achieved with the defocused technique. Other methods with lesser penetration of thermal effects (e.g. sp, scanner) do not reach the deeper-lying cells and, consequently, render higher rates of recurrences. Continuous smoking after surgical treatment and widespread multiple-focus lesions are the prognostic indicators for recurrence after laser surgery (8).

White et al. (9) retrospectively evaluated 39 patients with oral leukoplakia and concluded that CO_2 and Nd:YAG lasers were successful surgical options due to the minimal postoperative pain, minimally invasive therapy, and elimination of sutures.

METHODS AND RESULTS

Pubmed was searched in order to find out published papers in the last 20 years (1996-2016) regarding the usage of various lasers in the treatment of precancerous lesions of the oral cavity. Using the terms "laser" and "oral precancerous lesion" 27 articles were found in the searched period. Since the oral leukoplakia is the most precancerous condition in the oral cavity, next search was based on the terms "laser" and "oral leukoplakia" when 122 articles were found. Review articles and clinical trials written on the English language were included in presented systematic review.

DISCUSSION

Various treatment procedures for precancerous lesions in the oral cavity have been reported: excision surgery (10), electrocoagulation (11), cryosurgery (12), laser surgery (3-10), the local use of corticoids and administration of vitamin A (13). An objective of the treatments for precancerous le-

sions of the oral cavity is to completely inhibit cell proliferation, or the disappearance of potentially neoplastic cells in the lesion, because there is a possibility of recurrence and/or malignant transformation from those cells (4). Excision surgery removes abnormal cells and causes postoperative scarring (10). Electrocoagulation produces thermal damage in the underlying tissue, which causes postoperative pain, edema and leads to considerable scarring (4). Cryosurgery causes tissue necrosis by freezing intra- and extracellular free fluid (4, 12). The absorbed energy by laser surgery causes vaporization of the intra- and extracellular fluid and destruction of the cell membranes (4-9). The CO_2 laser is the most used laser on the oral cavity during the past decade because of its affinity for water and high absorption by the oral mucosa. The use of the CO_2 laser does not reduce the risk of relapses of the lesion, but it is an easy-to-use technique and results in both a quick surgical procedure and trouble-free postoperative period and may be safely used in dental practice (14).

Oral leukoplakia

Leukoplakia is defined as „A white plaque or patch of questionable risk having excluded (other) known diseases or disorders that carry no increased risk for cancer" (15). The estimated prevalence of oral leukoplakia worldwide is approximately two percent (2, 4). There are some geographical differences with regard to the gender distribution. Leukoplakia is much more common among smokers (2). An annual malignant transformation rate is of approximately 1% is probably a realistic figure for all clinically and/or histopathological types of oral leukoplakia together. Risk factors of statistical significance for malignant transformation of oral leukoplakia are female gender, long duration of lesion, no-smokers, location on the tongue and floor of the mouth, size, non-homogeneous type, epithelial dysplasia and DNA aneuploidy (16). The most commonly used treatment modalities consist of surgical excision or CO_2 laser therapy. Recurrence rates after any type of treatment may vary from almost zero to up to 30%, probably mainly depending on the length of follow-up (2).

Diode laser

Fornaini et al. (17) compared four diode laser wavelengths (810, 980, 1470 and 1950 nm) for the ablation of the bovine tongues and significant temperature increase was recorded by 980 nm laser and the lowest by 1950 nm laser. The same authors concluded that the incision was better and tissue injuries were minor in the specimens obtained with higher wavelength (1950 nm) and at lower power (2W). Other group of authors (18) found wavelength of 810 nm to be potentially the best choise int he oral soft tissue surgery. Kundoor et al (19) reported satisfactory clinical results after treatment of oral leukoplakia and oral lichen planus using diode laser.

Carbon dioxide laser

Mogedas-Vegara et al. (8) performed a systematic review of the 33 papers (published between the years 1981. and 2015.) to evaluate treatment of oral leukoplakia with the carbon dioxide (CO_2) laser. The same authors concluded that CO_2 laser is excellent in the oral leukoplakia treatment due to its effectiveness and low associated morbidity, however, randomized clinical trials are needed to compare CO_2 laser with other surgical lasers.

Huang et al. (20) treated 22 patients with oral leukoplakia and 18 patients with oral lichen planus. Two patients with oral leukoplakia showed recurrence after the surgery, whereas there was no recurrence after laser. Therefore, the same authors concluded that CO_2 laser in the treatment of oral mucosal lesions has the advantages in terms of reduced bleeding, a clear view during surgery, and a shorter operative time.

Tambuwala et al. (10) treated 30 patients with oral leukoplakia by use of CO_2 laser and scalpel and concluded that CO_2 laser showed superior results when compared to the scalpel regarding better intra-operative and reduced scarring. There were no differences between CO_2 laser and scalpel regarding post-operative pain and swelling after laser excision did not show any significant difference from that of scalpel.

Lopez-Jornet et al. (21) compared conventional surgery with carbon dioxide (CO_2) laser in 48 patients with oral leukoplakia with regard to the postoperative pain and swelling and concluded that the CO_2 laser causes only minimal pain and swelling, making it as a valuable method to conventional surgery in treating patients with oral leukoplakia.

Lim et al. (22) reported that the use of KTP (potassium-titanyl phosphate) lasers for the treatment of oral leukoplakia may result in lower recurrence rates than when using CO_2 lasers.

Schoelch et al. (23) treated 39 patients with some degree of microscopic dysplasia and six which demonstrated high-risk proliferative verrucous leukoplakia by applying CO_2 and Nd:YAG lasers. None of the complications occurred except that two patients developed pyogenic granulomas in their surgical sites. Twenty-nine patients had complete control of their lesions; 19 patients had small recurrences; 2 patients had complete recurrences; and 5 patients developed squamous cell carcinoma at the lesion site. Verrucous lesions had an especially high rate of recurrence (83%), with 9 of 12 ultimately controlled with subsequent surgeries.

Deppe et al. (24) evalutaed the recurrence rate resulting from different methods after CO_2 evaporization. In that study 148 premalignant lesions were treated. Statistically significant lowest recurrence rates were yielded by the defocused cw-technique followed by the cw-scanner and the sp-mode. The results indicated that the best results when treating premalignant lesions of the oral mucosa can be achieved using defocused technique of CO_2 laser while other methods with lesser penetration of thermal effects do not reach the deeper-lying cells and, consequently, render higher rates of recurrence.

Brouns et al (25) in their cohort study on 35 patients found that the annual recurrence rate of oral leukoplakia treated with CO_2 laser was approximately 8%, which is significantly higher then in previous literature. Next year the same authors published another paper (26) on the topic of malignant transformation of oral leukoplakia in sample of 144 patients. They found that malignant transformation occured in 11% of patients, and concluded that annual malignant transformation rate is approximately 2.6%. they also found that the large size of lesion showed to be the only statistically significant predictor of malignant transformation of the oral leukoplakia. Similar rate of malignant transformation (10.4%) was observed in the study of Jersej et al. (27). The same authors observed the recurrence rate of approximately 19.5% after CO_2 laser surgery. Another group of authors (28) found lower recurrence rate (15%) after treating the oral leukoplakias with the same laser technique.

Neodymium-doped yttrium aluminium garnet laser

Vivek et al. (29) treated 28 patients with histologically proven leukoplakia by use of Nd:YAG laser and patients had only mild to moderate pain, swelling and restricted mouth opening, which peaked between 72 h and 1 week. Cure rate was 92.86% in a 6-month period. Longer period of postsurgical follow-up reported Tewari et al. (30) and Das et al. (31) with similar clinical results and successful rate. Montebugnoli et al. (32) in their prospective study observed that clinical healing of leukoplakia treated by Nd:YAG laser surgery may be accompanied by altered cell turnover in 20% oft he cases.

Erbium-doped yttrium aluminium garnet laser

There are only two reports on the use of Er:YAG laser in the treatment of oral leukoplakia (33, 34). Meister et al. (33) used Er:YAG laser to treat leukoplakia of the buccal mucosa which was completely ablated and complete remission was seen.

Earlier clinical study by Schwartz et al. (34) compared the efficacy of Er:YAG and CO2 laser in oral leukoplakia ablation, where authors concluded that the both treatment modalities still have some limitations to achieve predictable eradication of oral leukoplakia.

Erbium, chromium: yttrium-scandium-gallium-garnet

In comparison to the scalpel surgery one might suspect that lesions removed with lasers could not be utilized for histopathology analyses. However, Seoane et al. (35) concluded that irradiation with Er,Cr:YSGG laser induces a minimal amount of thermal artifacts at the surgical margins of oral leukoplakias and avoids diagnostic interferences with real dysplastic borders.

Oral lichen planus

Oral lichen planus is generally regarded to represent a potentially malignant disorder. The reported annual malignant transformation rate is probably less then 0.5%. the issue of malignant

transformation in oral lichen planus is blurred by the lack of clinicopathologic correlation in the diagnosis. The efficacy of continuous follow-up of oral lichen planus patients is questionable (2)

Misra et al. (36) treated patient with OLP lesions using diode laser (940 nm) and there was complete remission of painful OLP symptoms. De Magalhaes et al. (37) treated patients with OLP by use of CO_2 laser in order to remove lesion and after one year there were no signs of recurrence. Therefore, the same authors concluded that CO_2 laser is useful for the tretament of oral lichen planus. Furthermore, van der Hem et al. (38) treated 21 patients with 39 OLP lesions by use of CO_2 laser and after 1-18 years at follow-up visit, 21 were painless and 6 patients had painful OLP recurrence. Previously all these patients were unresponsive to the golden standard with corticosteroid treatment and therefore the same authors suggest CO_2 lasers in the tretament of painful OLP lesions.

Fornaini et al. (39) used Er:YAG laser in two patients with OLP were as follows: energy, 80-120 mJ; frequency, 6-15 Hz; non-contact hand piece; spot size diameter, 0.9 mm; pulse duration, 100 μsec (VSP) to 300 μsec (SP) ; fluences, 12.6-18.9 J/cm(2); and air/water spray (ratio: 6/5). A very small OLP recurrence was seen in one patient after 15 months. On the other hand, Agha-Hosseini et al. (40) reported that low-level laser therapy was superior to CO_2 laser with regard to the size of OLP lesions and pain.

Erythroplakia

Erythroplakia is defined in a similar way as leukoplakia, being a "A fiery red patch that cannot be characterized clinically or pathologically as any other definable disease." The clinical appereance is often a flat or depressed erythematous change oft he oral mucosa. Erythroplakia needs to be treated because of its high risk of malignant transformation. Most of the lesions are symptomatic. Surgery, either a cold knife or by laser excision is the recommended treatment modality- there are no data from the literature about the recurrence rate after excision of erythroplakia (2).

Yang et al. (41) treated 84 patients with invasive carcinoma (n=3), dysplasia/carcinoma in situ (n=61), and squamous hyperplasia (n=20) by carbon dioxide laser excision. There was no postoperative malignant transformation, but invasive carcinoma found after initial excision (n=3) was treated by further radical excision. The same authors (42) concluded that laser excision is effective in treating oral erythroplakia that is still confined to dysplasia of any degree, with low morbidity. The area of oral erythroplakia is a predictive factor for postoperative recurrence.

Cantarelli Morosolli et al. (43) treated patient with erythroleukoplakia involving the lower lip CO_2 laser with 0.8 mm focus, 5 W, power density of 2.5 W/cm^2 in continuous mode. After 6 months, no recurrence was seen.

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