A Comparative Evaluation of Diode Laser Ablation versus Scalpel Excision for Management of Oral Leukoplakia

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Abstract

Background and Aim: Oral leukoplakia, a potentially malignant disorder with malignant transformation rate ranging from 0.6% to 20%, requires immediate attention. Therefore, for moderate to severe dysplasia, complete surgical removal is the treatment modality. This study aimed to evaluate two treatment modalities of oral leukoplakia using diode laser and scalpel surgery and to compare the outcome of both interventions regarding postoperative pain and functional disturbances. Materials and Methods: A total of 30 patients with oral leukoplakia were recruited and block randomization was done splitting into diode and scalpel groups. Patients were evaluated for pain and functional disturbances postoperatively using visual analog score (VAS) and Gorsky criteria, respectively, in the first 3 days and 1st, 2nd, and 4th weeks and periodically followed up for 4 years for recurrences. Results: The mean age was 38 years. The results showed a significant difference in diode group compared with scalpel group for postoperative pain assessed in VAS scale using paired "t"-test and functional disturbance using Chi-square test. None showed recurrence in the subsequent 4 years of follow-up among diode, whereas scalpel group showed recurrence in two patients. Conclusion: Complete resolution of the lesion with minimum patient discomfort was observed in patients treated with diode compared with scalpel, suggesting diode laser is an effective method over the conventional method.

Keywords: Diode laser, leukoplakia, scalpel excision

INTRODUCTION

Oral cancer is one of the 10 most common cancers in the world with a delayed clinical detection, poor prognosis, without specific biomarkers for the disease, and expensive therapeutic alternatives.[1] Therefore, the burden of oral cancer among the public health in India is greater. The amenability of the oral cavity for visual inspection and the availability of established clinically defined precursors (leukoplakia, erythroplakia, and oral submucous fibrosis) provide an ideal opportunity for early detection and secondary prevention of squamous cell carcinoma (SCC) as it constitutes about 90% of oral malignancies, with a ~50% survival rate over 5 years despite various treatments.[2]

The focus, therefore, has shifted toward early diagnosis and prompt treatment of these lesions for improving the prognosis.[3] Oral leukoplakia is a commonly seen potentially malignant lesion with varied clinical presentation with global prevalence varying from 0.5% to 3.4% and malignant transformation ranging from 0.6% to 20%.[4] These potentially malignant disorders (PMD) cannot be differentiated from early oral cancers by visual examination alone regardless of the expertise of the clinician.[3] Many innocuous appearing at early stage oral cancerous lesions are merely observed clinically and left undiagnosed, and hence various adjunctive and noninvasive tools have been developed at both clinical and molecular levels to assess the oral lesions of uncertain biologic significance.[3] One such technique is vital staining including toluidine blue which is a basic metachromatic dye that stains the acidic cellular components. Since cancer cells contain

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quantitatively more DNA and RNA than normal epithelial cells, toluidine blue delineates areas of malignancy.\(^6\) It is a simple, fast, and inexpensive technique.

In the present literature, various treatment modalities have been proposed with varied success rates. Pharmacotherapy using vitamin A analogues (retinoids) and other antioxidant vitamins and nutrients (i.e. beta carotene, vitamins C and E) have not been effective in well-designed, prospective studies. The theory is that antioxidants help stabilize cellular free radicals (mainly unstable oxygen) that can serve as promoters of chromosomal mutagenesis and carcinogenesis.\(^7\) Problems in chemoprevention involve toxicities during administration and recurrences when the drug is discontinued. So surgical removal is a definitive treatment in moderate to severe cases.\(^7\) Hence, definitive treatment of oral leukoplakia is very important because of its recurrence and malignant transformation.\(^8\) Among various surgical treatments, laser techniques have helped improve surgical approaches and ultimate control of leukoplakia. \(\text{CO}_2\) laser, Erbium family laser, neodymium: yttriumaluminum garnet (Nd: YAG) laser, and diode laser are mainly used for the elimination of the tissues, but mainly diode laser because of its portable nature and ease of use for minor soft tissue surgery, cost-effectiveness is gaining wide acceptance in dentistry. Hence, diode laser is very commonly used in many surgical procedures and has many advantages such as reduced scar formation, less pain and bleeding, and reduced chances of infection.\(^9\) Many researchers have also found that diode laser can be used to eliminate benign, potentially malignant disorders of the oral soft tissues.\(^9\) There are only fewer studies available in the present literature regarding usage of diode laser in the management of potentially malignant disorders. So, diode laser ablation for leukoplakia as a definitive treatment modality was chosen for treatment and compared with conventional scalpel excision.

The aim and objectives of this study were first to evaluate the efficacy, safety, and the acceptability of the diode laser in the management of oral leukoplakia and to compare that with conventional scalpel excision, and second to evaluate the nature of postoperative adverse effects, if any, associated with laser ablation and scalpel within consecutive 1, 2, and 3 weeks and 1 month of follow-up and also to check for any recurrences within a follow-up period of 4 years.

**Materials and Methods**

Patients with clinical diagnosis of leukoplakia were recruited from the Department of Oral Medicine and Radiology, AECS Maruti College of Dentistry, Bengaluru, in a span of 2 years using convenient sampling after obtaining institutional clearance. The patients who were willing to participate, quit the habit, give consent, and with an age range between 20 and 60 years were included in the study. The patients who were not willing to stop adverse habits and to give consent, and with any other systemic diseases were excluded from the study [Figure 1].

Patients were advised to discontinue all the adverse habits and counseling was done, followed by complete physical head and neck examination and they were advised to use topical clotrimazole over the affected site for 1 week to manage and rule out any superadded candidiasis. After 1 week, punch biopsy was performed under local anesthesia prior to treatment. Leukoplakia patients with moderate to severe dysplasia were included in the study after clinical and histopathological confirmation. Informed consent was obtained before inclusion in the study. The lesions were classified according to the size. All surgeries were performed by the same surgeon and carried out under 2% lidocaine with 1:100,000 adrenalin.

The patients were randomized into two groups. Block randomization was done considering factors such as age,
gender, extent of lesion, and dysplasia to ensure balance between two treatment arms, that is, diode and scalpel. Randomly generated treatment allocation sequences were concealed in a sealed opaque envelope to eliminate bias. Group 1 was treated with diode laser ablation and the wound was left open for healing by secondary intention. Group 2 was treated with scalpel excision followed by 3/0 sterile mersilk suture used to heal by primary intention.

Before starting the surgery, the lesional area was dried with the help of gauze piece and toluidine blue staining was performed. The retention of stain regardless of the intensity was defined as “positive” test and absence of any stain was defined as “negative” test. After this procedure, the patients were infiltrated with local anesthesia and personal protection barriers were used for both staff and patients under strict aseptic conditions.[3] Then the lesion was irradiated by diode laser K-Laser professional 6SE (diode laser) (970 ± 15 nm, 300 µm contact mode, 6 W) till the area changed to white, that is, photocoagulation (contact mode, pulse mode). Remnants of the ablated tissue were removed using sterile gauze dampened with saline solution. The procedure was carried out further till the desired depth of tissue was removed along with the surrounding 2 mm of the normal tissue. In the scalpel excision group, a wide and shallow excision was done covering the positive areas followed by sutures placed, and postoperative instructions were given and analgesic was prescribed. After 1 week, the patients were recalled for suture removal.

All cases were examined in the first 3 days, and 1, 2, and 4 weeks after surgery by a third person who was blinded to the study. Clinical evaluation of postoperative complications such as bleeding, swelling, functional disturbance, and wound healing was done using visual analog score (VAS)[4] and subjective evaluation was done according to Gorsky and Raviv (1992).[13] A VAS of 100 mm in length was used to evaluate the intensity of pain and swelling. This scale converted the visual analogical evaluation made by the patient into a numerical value: from 0 (corresponding to 0 mm on the VAS and showed no pain and no swelling) to 10 (100 mm on the VAS and showed unbearable pain and maximal swelling). Postoperative complications such as pain, bleeding, edema, and functional disturbances were graded 0–10 according to the following:

- 0–2: no postoperative complications
- 3–5: mild postoperative complications
- 6–7: moderate postoperative complications
- 8–10: severe postoperative complications

The patients were continuously monitored periodically for 4 years to evaluate for any recurrences. Recurrence was considered to be a leukoplakia arising in the excised site as the first or within the borders of the treated area. To evaluate the recurrence rate in and around the surgical site, we included only patients with a minimum follow-up of 6 months.

Data were analyzed using SPSS version 12.0 statistical package. A descriptive study was done for each variable. Student’s t-test was carried out for comparison and Chi-square test for nonparametric variables.

**Results**

A total of 128 patients diagnosed with leukoplakia were screened for a period of 2 years. Among them, 98 patients were excluded as shown in Figure 1, and a total of 30 were included in this study. Of the 30 patients, 2 were females and the rest were males with a mean age of 38 years. Of these, 18 patients had single-site lesion with a high prevalence for buccal mucosa and 12 patients had bilateral lesion on retrocommissural area. Among 30 patients, 28 showed classical homogeneous leukoplakia with moderate epithelial dysplasia and 2 showed speckled leukoplakia with severe epithelial dysplasia. All the patients were subjected to topical toluidine blue application which gave 100% sensitivity for the positive sites and also slightly adjacent to the clinically observed lesion in patients especially with inhomogeneous leukoplakia.

The laser ablation group did not show difficulty while operating, and pain disappeared by the end of first week. In the scalpel group during excision, especially in few patients with wide lesions, there was difficulty in approximating the suture ends; postoperatively, in the first 3 days, there was severe pain, and at the end of 1 week 13% of patients still showed moderate pain. On comparing both the groups on 3rd and 7th days postoperatively, there was a statistically significant difference ($P = 0.001$), suggesting that diode group experienced lesser pain. On 2nd and 4th weeks, both the groups experienced no pain [Table 1].

Bleeding was more in the scalpel group (60%), whereas in the diode group there was minimal to no bleeding. Edema occurred in both the groups in the first 3 days of postoperative follow-up. The diode group experienced comparatively less edema than the scalpel group in the subsequent visits, which showed statistical significance ($P = 0.001$). Nevertheless, by the end of first week, edema was subsided completely in both the groups [Table 2].

Functional disorder occurred in some patients which was mainly in direct relation to the degree of pain and edema. On 3rd day comparison, there was statistical significance ($P = 0.001$), suggesting that the diode group experienced less functional disturbances which returned to normal function with complete remission of lesion [Table 3], and there was no postoperative bleeding or scar formation and the lased area was soft on palpation and benefited with the treatment. At the end of 1 week, the scalpel group exhibited minimal functional disturbances signifying that diode laser ablation was more acceptable with minimal complications compared with scalpel. Gorski criteria showed that both the groups benefited in spite of modality, but the diode group showed 80% clinical remission within the first few days [Table 4].

Periodic follow-up was done for every 6 months till 4 years wherein none of the diode group showed recurrence, neither
Table 1: Pain

| Group     | Mean      | T     | P     |
|-----------|-----------|-------|-------|
| Day 3     | Diode     | 4.67±1.5 | −7.379 | 0.001* |
|           | Scalpel   | 7.33±0.6 |       |       |
| Week 1    | Diode     | 0.13±0.4 | −7.897 | 0.001* |
|           | Scalpel   | 2.00±1   |       |       |
| Week 2    | Diode     | 0       |       |       |
|           | Scalpel   | 0       |       |       |
| Week 4    | Diode     | 0       |       |       |
|           | Scalpel   | 0       |       |       |

*Significant

Table 2: Swelling

| Group     | Mean      | T     | P     |
|-----------|-----------|-------|-------|
| Day 3     | Diode     | 2.53±1.5 | −1.439 | 0.001* |
|           | Scalpel   | 3.53±2.3 |       |       |
| Week 1    | Diode     | 0.20±0.4 | 1.871  | 0.07   |
|           | Scalpel   | 0       |       |       |
| Week 2    | Diode     | 0       |       |       |
|           | Scalpel   | 0       |       |       |
| Week 4    | Diode     | 0       |       |       |
|           | Scalpel   | 0       |       |       |

*Significant

Table 3: Functional disturbances

| Group     | Mean      | T     | P     |
|-----------|-----------|-------|-------|
| Day 3     | Diode     | 5.20±2 | −2.678 | 0.01* |
|           | Scalpel   | 6.87±1.4 |       |       |
| Week 1    | Diode     | 1.27±0.7 | −2.928 | 0.007* |
|           | Scalpel   | 2.20±1 |       |       |
| Week 2    | Diode     | 0       |       |       |
|           | Scalpel   | 0       |       |       |
| Week 4    | Diode     | 0       |       |       |
|           | Scalpel   | 0       |       |       |

*Significant

Table 4: Gorski criteria for Subjective evaluation

| Clinical indicator | Group | Chi-square | P     |
|-------------------|-------|------------|-------|
| Stage 1            | Diode | 4.316      | 0.229 |
| (30%-50% improvement) | Scalpel | 1 (6.7%) |       |
| Stage 2            | Diode | 1 (6.7%)   |       |
| (50% benefit)      | Scalpel | 1 (6.7%) |       |
| Stage 3            | Diode | 2 (13.3%)  | 6 (40%) |
| (70%-80% benefit)  | Scalpel | 2 (13.3%) |       |
| Stage 4            | Diode | 12 (80%)   | 7 (46.7%) |
| (90%-100% remission of sign and symptoms) | Scalpel | 12 (80%) |       |
| Stage 0            | Diode | 0         | 0     |
| (Little improvement/no change) | Scalpel | 0     |       |

*Significant

new lesions nor malignant transformation. Whereas in the scalpel group, 20% (n = 3) of the patients showed recurrence of the lesion in the excised area [Table 5].

**Discussion**

In potentially malignant disorders, which are manageable with chemoprevention, toxicity is considerable and also relapse is common after discontinuing.[14-16] One such study using retinoic acid for oral leukoplakia showed that molecular abnormalities persist in few patients with clinical response, suggesting chemoprevention delays rather than preventing carcinogenesis.[17] Hence, surgical excision is recommended especially in oral leukoplakia with moderate to severe dysplasia according to Arruda et al.[17]

As laser treatment offers many advantages in both intraoperative and postoperative periods, such as ultimate control of leukoplakia without any wound contractures, profound control over bleeding (hemostasis), healing, bactericidal effect, and improved patient compliance, it was selected as one of the treatment arms and compared with the conventional scalpel excision. It is also recommended that the patients must necessitate continued clinical monitoring following a surgical intervention to evaluate any reoccurrence or malignant transformation.[18]

Among various lasers available, diode laser is cost-effective, user-friendly, and can be used in contact mode. Its active medium is a solid semiconductor with wavelength ranging from 800 and 980 nm which cannot be absorbed by the dental hard tissues. Hence, diode laser is safe for soft tissue surgeries and was used in our study.[19-21]

Prior to surgical excision, vital staining procedure gives us the proposed lesional area to be excised. Hence, we have performed preoperative vital staining with toluidine blue to reduce recurrences as it covers multicentric or microinvasive cancers. Chaudary et al.[3] in their study also showed high sensitivity value with respect to leukoplakia patients suggesting that prior vital staining is a valuable step for the selection of the area to be excised which is in accordance to our study. In this study, inhomogeneous leukoplakia presented a wide positive site for toluidine blue application and the rest presented no much difference to the clinically evident lesion. In this study, 100% sensitivity was observed which may be attributed to the lesser sample size.

Laser ablation for leukoplakia is a promising treatment, as it is more effortlessly performed than excision with a knife and its power of penetration reaches to about 1.5 mm as seen in this study. Application of diode laser at 6 W in defocused continuous mode will increase the temperature of the affected tissues to above 50°C and less than 100°C. This temperature will cause protein denaturation. The sign of protein denaturation is blanching of treated mucosa. Denaturation of protein means destruction at the affected area of the diseased epithelium. In addition, cytotoxic protein subepithelial lymphocytes are all denatured due to its deeper penetration. Risk of secondary infection could be minimized with the help of denaturation which acts as a dressing layer for the treatment site that may decrease pain. Due to the sealing of blood vessels and lymph vessels, ice packs should be applied to the treated area.[17]
Regarding postoperative recovery, it was uneventful except pain and edema which disappeared at the end of first week in the diode group, but the scalpel group showed mild pain in 2 weeks’ follow-up. Laser surgery has many advantages for both the surgeon and the patient, both during and after the operation and the surgeon has excellent visibility during the operation and this enables shortening of the operative time. Also, patients do not require a special method to stop bleeding after surgery and it is possible, as a rule, to leave the excised edges unsutured in the excision technique. This can be used even in patients who have a comprehensive lesion treated by an ablation technique without any dressing on the wound and this keeps functional disorders to a minimum. Scalpel excision in comparison to laser ablation showed more discomfort and pain with significant difference in the first few days of therapy suggesting that laser ablation is superior to scalpel excision.

According to Vasavi Krishnamurthy, Laser-assisted ablation is a more precise treatment with less postop discomfort for leukoplakia; our study is in accordance with this study. Pulsed mode is more comfortable than continuous wave mode which was similar to a study done by Rolf Brochers and hence pulsed mode was used in our study. According to a case report by Tatu et al., diode laser was performed for leukoplakic ablation at 7 W which establishes its efficacy in management of oral leukoplakia, and we followed the same method in this study which showed profound acceptance by patients in comparison to scalpel. There was no recurrence of lesion in the laser group within a span of first 3 months in our study, which supports the case reported by Prajwalit Kende et al., unlike a study done by Nilesh et al. where reoccurrence was seen in two patients (n = 10). Ultimate control of leukoplakia is more important to reduce the risk. Hence, diode laser is a definitive technique with marked clinical improvement with high degree of patient acceptance in comparison to scalpel excision.

Marek and Smucle concluded that malignant transformation of leukoplakia does occur even after laser ablation, and for this reason it is necessary to subject the patients to systematic follow-ups. Hence, we have done follow-up periodically once in 6 months up to 4 years. During this period, none showed neither recurrence nor malignant transformation with diode laser ablation which might be attributed to prior toluidine blue application for the selection of surgical site and precise handling of diode laser pulse mode application and also the location of the lesion. Whereas scalpel group, in spite of controlled measures, showed recurrence (20%) suggesting diode laser ablation is superior to scalpel excision. This may be attributed to the location of lesion and difficulty in excising wide lesions using scalpel.

According to Nilesh et al. and Ishii et al., laser ablation was a more precise removal with less postop complication, which is in accordance to our study. Also, patients do not require a special method to stop bleeding after surgery and it is possible, as a rule, to leave the excised edges unsutured in the excision technique which was according to Hirano et al. Ortega-Concepción et al. in their review, concluded that diode laser, being a safe and effective method for the excision of soft tissue lesions, was validated in our study.

This can be used even in patients who have a comprehensive lesion treated by a vaporization technique without any dressing on the wound and this keeps functional disorders to a minimum. According to a study done by Ioanina et al., comparison of recurrence rate between different laser techniques such as CO2 laser, Nd: YAG laser, and potassium-titanyl-phosphate (KTP) in the leisional area was about 34.2%, 28.9%, and 17%, respectively, whereas this study did not show any recurrence among laser group. This may be attributed to the location of the lesion determining recurrences and malignant transformation.

Mehana et al. in a systematic review of 14 studies reported that surgery may reduce transformations to malignancy of oral leukoplakia with dysplastic features, although it may not eliminate this risk completely despite complete removal using scalpel excision or laser vaporization. As the adjacent or peripheral epithelium may proliferate in the recurrence phenomenon, it is proposed that these epithelial tissues, which show clinically normal features, consist of highly active cells which are probably abundantly widespread in the basal cell layer. It has been accepted that “field cancerization” or “field change” of oral mucosal cancer is very important in explaining the presence of dysplastic cells adjacent to squamous cell carcinoma as well as potentially malignant disorders and recurrence following complete laser vaporization. Definitely, there is correlation between location of lesion, dysplastic activity, adverse habits, gender, and presence of lesion for longer duration.

**Conclusion**

Diode provides an alternative technique with marked clinical improvement and high degree of patient acceptance within the limits of this study. Because of good coagulation, patients’ surgical period with high-risk infections was reduced. Exceptionally precise tissue ablation at low power settings diode lasers is neither absorbed too much nor too little in water and haemoglobin, enabling precise char-free soft tissue ablation and hemostasis. The small portable size of the unit is of beneficial effect for the dentists. It is recommended that future studies can be carried out for evaluation of malignant transformation rate and recurrences with large sample size.

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Conflicts of interest
There are no conflicts of interest.

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