Original Article - Retrospective Study

Diode Laser in the Management of Leukoplakia - A Retrospective Study

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Abstract

Introduction: Leukoplakia is among the most common potentially malignant disorders encountered in clinical dental practice. The treatment of leukoplakia includes nonsurgical and surgical management. The surgical treatment includes excision, electrocauterisation, laser surgery or cryosurgery. This retrospective study aimed to analyse the efficacy of diode lasers in the management of leukoplakia. **Methods:** The sample consists of 56 cases with 77 leukoplakia sites treated with diode laser between January 2018 and December 2020 with a minimum of six months follow-up. For each patient, personal data was collected along with site of lesions, leukoplakia phase, type of treatment performed (laser ablation or laser excision), side effects, recurrences and malignant transformation. Inferential statistical analysis was then conducted. **Results:** After applying exclusion criteria, 56 cases with 77 leukoplakia sites were included in this study. Males aged >45 years were predominantly affected. Homogeneous leukoplakia (48.1%) was the most common phase. Recurrences were noted in 19.48% of the cases. Compared to laser excision, laser ablation had more recurrences. Gingival lesions showed a higher recurrence rate than other sites in the oral cavity. None of the cases showed malignant transformation. **Discussion:** Laser offers many advantages over other conventional methods including lesser postoperative pain and swelling, bloodless dry operating field and increased patient comfort and requires minimal local anaesthesia. The study concluded that diode laser is an effective surgical treatment modality for treating leukoplakia. Furthermore, the laser excision technique was found to be superior to laser ablation due to lesser recurrence.

Keywords: Diode laser, laser ablation, laser excision, leukoplakia, potentially malignant disorders

Introduction

Most types of oral cancers are preceded by clinical changes in the oral mucosa, usually as a white or red patch confirming the two-step cancer development process. In 2007, the World Health Organization recommended the term 'oral potentially malignant disorder' (OPMD) for such lesions in the oral cavity, which is defined as 'any oral mucosal abnormality that is associated with a statistically increased risk of developing oral cancer'.[1,2]

Leukoplakia is one of the most leading OPMDs encountered in clinics. The term 'leukoplakia' should be used to recognise the white plaques of questionable risk after excluding (other) known diseases or disorders that carry no increased risk for cancer.[1,2]

The treatment of leukoplakia begins with counselling for tobacco cessation in any form.[3] The non-surgical treatment includes chemopreventive agents, topical tretinoin/isotretinoin, topical bleomycin, 13-cis-retinoic acid and photodynamic therapy.[3,4] The chemopreventive agents/antioxidants are potent scavengers of free radicals, preventing free radical-induced carcinogenesis.[4,5] The main drawback of chemoprevention is its toxicity and recurrence when the drug/treatment is stopped.[6] Thus, surgical excision/removal is considered the best treatment, especially in moderate-to-severe cases, to

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prevent malignant transformation and recurrences. Surgical treatment includes excision surgery, electrocauterisation, laser surgery or cryosurgery.[7]

Light Amplification by Stimulated Emission of Radiation (LASER) uses optical amplification to create light using stimulated emission of electromagnetic radiation. The lasers described previously on the treatment of leukoplakia are as follows: CO_2 laser, Erbium-doped Yttrium Aluminum Garnet (Er: YAG) laser, Neodymium-doped Yttrium Aluminium Garnet (Nd: YAG), diode laser and Potassium titanyl phosphate (KTP) laser. CO_2 lasers have been used extensively for oral surgical procedures. However, the diode laser is advantageous owing to its compact size, portable nature and ease of handling/use in soft-tissue surgeries. It can also be used in contact mode and is cost-effective.[8]

Goharkhay *et al*. reported that the diode laser has better incision performance with a cutting depth of 2–6 mm and excellent coagulation ability compared to ND:YAG laser due to its better absorption property to haemoglobin. Compared to the CO_2 laser, the diode laser neither causes any lateral damage nor charring of bone below the soft tissue in continuous wave or pulsed mode at an average power of 4.5 W.[9]

Based on the depth of tissue removed and the presence of dysplastic features, leukoplakia can be treated by two techniques using lasers: (a) laser ablation (diode laser)/laser evaporation (CO_2 laser) for superficial removal of the lesion up to the epithelium and (b) laser excision for deeper removal of the lesion.[8-11]

Till date, only a few studies are reported on diode lasers in the treatment/management of leukoplakia. Therefore, in this study, we aimed to analyse the efficacy of diode laser in the management of leukoplakia. The objectives of the study were as follows: (a) to compare the effect of laser ablation and laser excision for the treatment of leukoplakia, (b) to deduce the recurrence rate after laser treatment and (c) to assess the malignancy transformation rate after laser treatment.

Materials and Methods

This retrospective study was carried out in the Department of Oral Medicine and Radiology at Nobel Medical College Teaching Hospital, Biratnagar, Nepal. The World Medical Association's Declaration of Helsinki on Ethical Principles for Medical Research involving Human Subjects was followed in all aspects of the study's protocols. The Institutional Ethics Committee's (IRC-NMCTH 567/2021) permission was obtained for the study. The present research was done in line with the Strobe Statement (strobe-statement.org).[12]

Study population, setting and design

The information was gathered from patient clinical records submitted to the Departments of Oral Medicine and Radiology of Nobel Medical College Teaching Hospital in Nepal between January 2018 and December 2020. It was a single-centre, retrospective inferential research.

Inclusion criteria

Patients with leukoplakia treated with a diode laser with minimum 6-month follow-up were included in the study.

Exclusion criteria

Subjects with incomplete treatment and cases with no follow-up observation for at least 6 months were excluded from the study.

Treatment protocol

The clinical records of the patient population with the same laser treatment protocol were selected. A detailed personal history regarding the adverse habits and examination of the lesion was assimilated. The vital staining was performed in all cases using toluidine blue. The stain at the site, regardless of its intensity, was considered a 'positive' test, while the absence of stain was considered a 'negative' test. Toluidine-positive patients and cases suspected with dysplasia-like speckled leukoplakia and those about 200 mm^2 were sent for biopsy. Finally, leukoplakia cases with negative toluidine blue staining and cases without dysplasia and gingival lesions were selected for laser ablation, while cases with mild and moderate dysplasia and cases of the sites of high risk of malignant potential such as floor of mouth and tongue were treated with laser excision.

The ill effects of adverse habits were explained to all the patients. They were motivated and advised to quit such habits by way of the 5A principle (Ask, Advise, Assess, Assist and Arrange). The antioxidants were advised as chemoprophylactic measures for a month. According to the routine protocol, we recommended topical anti-fungal agents for 10 days before the laser treatment. Patients not responding to the initial measures were treated with laser.

In this study, perilesional infiltration of local anaesthetic was applied. A diode laser at 980-nm wavelength (Ga-Al-As, DILAS, Germany) (Model: IndiLase, MEDSOL, Hosur, India), operating in a continuous mode with an output power of 2.0–4.0 W and a flexible 400mm diameter optic fibre (polyamide, 400 microfibers; Medfibers) equipped with a handpiece, was used. The energy produced at the target site varied according to the size of the lesion. Typically, the energy transmitted to the tissue was 1600–3200 J/cm^2. The aseptic conditions were maintained, and protective eyeglasses were given to both patients and operators.

Laser ablation

Laser ablation is the superficial removal of the lesion, including a margin of clinically healthy mucosa. Some basic points which were taken into consideration:[8] (a) 3–4 mm of the surrounding healthy tissue with 1 mm in depth was involved; (b) wherever the distance between two lesions was ≤6 mm, both areas were considered one large lesion and (c) a demarcation line was marked with laser to limit the ablated tissue [Figure 1].

Laser excision

The first incision was made at a depth of ≥3 mm (depending on the size and site of the lesion), followed by excision at

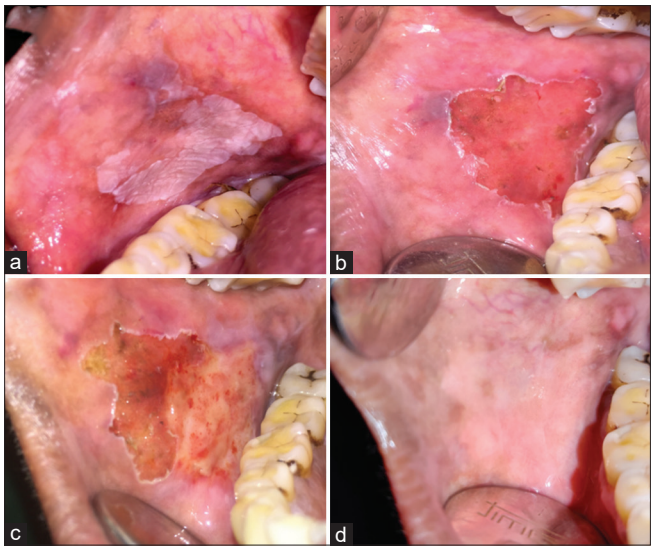

Figure 1: Case of leukoplakia treated by laser ablation: (a) Leukoplakia on the right buccal mucosa, before treatment, (b) Immediate post-operative view, (c) Two weeks after laser resection, (d) Complete healing after 1–1.5 months

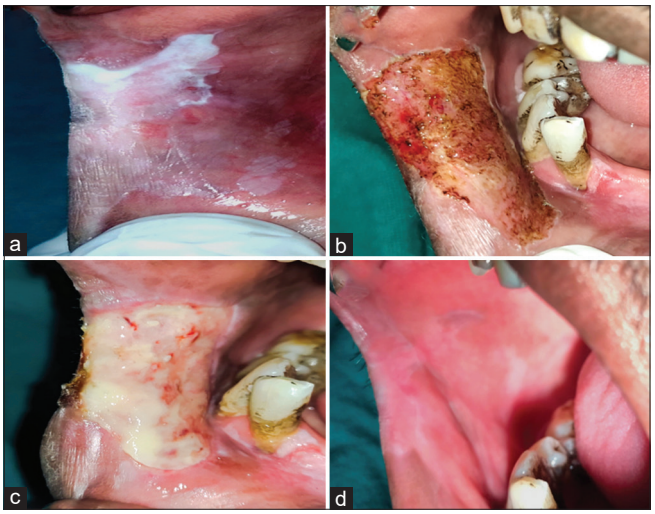

Figure 2: Case of leukoplakia treated by laser excision: (a) Leukoplakia on the right retrocommissural area, before treatment, (b) Immediate postoperative view, (c) Two weeks after laser resection, (d) Complete healing after 2 months

3–4 mm depth by undercutting the tissue. The tissue excised with the laser was subjected to a detailed histopathological investigation. The surgical wound was left unsutured and allowed to heal by secondary intention [Figure 2].

After laser surgery, the postoperative instructions for wound care, diet and post-operative drugs including antibiotics and non-steroidal anti-inflammatory drugs were prescribed to all the patients.

Confounders, variables and assessment

The following variables – age, sex, gender, site of lesions, phase of leukoplakia, type of treatment performed (laser ablation or laser excision), side effects, recurrences and malignant transformation – were studied. Recurrences based on the site and types of treatment were also tabulated.

Statistics

The collected data were analysed with IBM SPSS statistics software version 24.0 (IBM Inc., Chicago, Illinois, USA). Descriptive statistics (mean, median and standard deviation) were used to describe continuous data. Student's *t*-test was used for parametric continuous data, while Chi-square testing was used for categorical data. $P < 0.05$ was considered statistically significant.

Results

A total of 86 case records of leukoplakia treated with diode laser were identified. After applying exclusion criteria, 56 cases with 77 leukoplakia sites were included in this study. Among them, 39 (70%) subjects were male and 17 (30%) were female. The patients ranged from 28 to 77 years, while 66% of the selected subjects were aged >45 years [Table 1].

Of the 77 clinically confirmed lesions, 18 (23.4%) were pre- or thin leukoplakia, 37 (48.1%) were homogeneous leukoplakia, 8 (10.4%) were proliferative verrucous leukoplakia and 15 (19.5%) were speckled leukoplakia; homogeneous leukoplakia was the most common type in the present study [Table 1].

Table 1: Details of age, gender and phase of leukoplakia

	Frequency (%)
Details of age	
25-45	19 (33.9)
>45	37 (66.1)
Total	56 (100)
Details of gender	
Male	39 (69.6)
Female	17 (30.4)
Total	56 (100)
Details as per the phase of leukoplakia	
Pre-leukoplakia	18 (23.4)
Homogeneous leukoplakia	37 (48.1)
Proliferative verrucous leukoplakia	8 (10.4)
Speckled leukoplakia (only mild/moderate dysplastic lesion)	15 (19.5)
Total	77 (100)

Furthermore, the most common lesions were observed in the buccal mucosa (28.6%), followed by gingiva, vestibule, tongue, retro-commissural area, labial mucosa, the floor of the mouth and palate [Table 2].

Based on toluidine blue test and biopsy, a total of 51 (66.2%) lesions were subjected to laser ablation, while laser excision was performed in 26 (33.8%) lesions [Table 3].

Initially, a complete remission of all the lesions was observed with both laser ablation and laser excision, but recurrence was noted in 19.48% of the cases over an average period of 4–6 months. Compared to laser excision (7.6%), laser

Table 2: Details of site of involvement and their recurrences

	Frequency (%)	Recurrences (%)
Buccal mucosa	22 (28.6)	2 (9)
Tongue	9 (11.7)	2 (22.2)
Gingival	10 (13.0)	5 (50)
Vestibular areas	10 (13.0)	2 (20)
Retrocommissural area	9 (11.7)	1 (11.1)
Upper labial mucosa	3 (3.9)	0
Lower labial mucosa	4 (5.2)	1 (25)
Hard palate	4 (5.2)	1 (25)
Floor of mouth	4 (5.2)	1 (25)
Retromolar area and soft palate	2 (2.6)	0
Total	77 (100)	15 (19.4)

Table 3: Detailed comparison of laser ablation and laser excision in terms of side effects and recurrences

Variables	Laser ablation (%)	Laser excision (%)	Statistical value (Chi square/ *t* value, *P*-value)
Details of the type of treatment performed			
Number of lesions	51 (66.2)	26 (33.8)	-
Details of the side effects			
Post-operative pain	51 (100)	26 (100)	χ^2=0 *P*=1 (NS)
Oedema	10 (19.6)	16 (61.5)	χ^2=2.838 *P*=0.092 (NS)
Scaring formation	0	5 (19.23)	χ^2=0.766 *P*=0.451 (NS)
Granuloma formation	0	1 (3.8)	χ^2=0.096 *P*=0.822 (NS)
Mean VAS scale on 3rd post-operative day	4.15±0.57	6.07±0.87	*t*=2.662 *P*=0.047 (NS)
Infection	0	0	-
Malignant transformation	0	0	-
Recurrences	13 (25.5)	2 (7.6)	χ^2=3.477 *P*=0.062 (NS)

NS: Not significant, VAS: Visual Analogue Scale

ablation (25.5%) had more recurrences. In addition, gingival lesions showed a higher recurrence rate than other sites in the oral cavity. The details of site of involvement and their recurrences are summarised in Table 2.

The comparison of the side effects between laser ablation and laser excision groups revealed that mild-to-moderate post-operative pain was observed in all the patients, while oedema, scarring and granuloma formation were frequently observed in the laser excision group, but the relation was non-significant. The relation of the mean Visual Analogue Scale (VAS) score on the 3rd post-operative day for the laser ablation and laser excision was found to be significant (P = 0.047). None of the cases showed infection and malignant transformation following laser treatment. These side effects are summarised in Table 3.

Discussion

Various medical and surgical treatments have been employed to exterminate leukoplakia, but it is challenging to eradicate these disorders due to the chances of relapse and incomplete elimination. Previous literature suggested topical retinoid as the medical management of leukoplakia, but recurrences have been reported after withdrawal in approximately 50% of the cases.[13] Various surgical modalities available for leukoplakia are laser therapy, cryosurgery and conventional scalpel surgery.[7]

Laser offers many advantages over other conventional methods: lesser post-operative pain, bloodless dry operating field, bactericidal effect, increased patient comfort, lesser chances of scarring, lesser post-operative swelling and minimal local anaesthesia. Moreover, previous studies confirmed that laser surgery had a lesser recurrence rate than scalpel surgery.[14,15]

A comparative study between diode laser, CO_2 laser and cryotherapy showed that diode laser and CO_2 laser had better clinical outcomes of parameters, such as pain, oedema and slough formation than cryosurgery in the management of leukoplakia. Pain was significantly higher in CO_2 laser and surgery group as compared with diode laser group over a period of 2 weeks. Pain was evaluated with the help of VAS, while oedema was evaluated by comparing the wound area with the anatomical area of the opposite side for the presence or absence of asymmetry.[16]

A regular follow-up is mandatory for these cases to evaluate any recurrences. According to the 'recurrence phenomenon', the adjacent clinically normal peripheral epithelial tissues contain abundant active cells in the basal cell layer. These active cells might proliferate in the future to cause recurrences. It is commonly acknowledged that 'field cancerisation' or the so-called 'field change' of cancer plays a significant role in the occurrence of dysplastic cells close to the oral squamous cell carcinomas and other OPMDs. It also explains the events of recurrence following complete laser vaporisation.[11] Laser ablation has more chances of recurrences compared to excision cases.[15]

Previous studies of leukoplakia treated with laser by Ishii *et al*.[11] and Yang *et al*.[17] showed a recurrence rate of 29.3% and 17.5%, respectively, while a meta-analysis by de Pauli Paglioni *et al*.[18] concluded that the overall recurrence rate was 16.5%. Herein, we observed a recurrence rate of 19.48% (15/77 lesions). The recurrence rate was higher for laser ablation compared to laser excision. Moreover, the gingival lesion showed a maximum recurrence rate (50%) compared to the other sites.

Laser ablation has a high recurrence rate possibly related to incomplete deep removal, as described above. Gingiva had the highest recurrences as laser excision was not performed in any case due to the limited thickness available. Recurrences may

also be related to patient's gender, non-cooperation to quit the habit, dysplastic activity, location of the lesion and the presence of lesion for a prolonged period.[14]

A study by Ishii *et al*.[11] reported malignant transformation in leukoplakia occurring even after laser evaporation, thereby necessitating systematic follow-ups for the subjects. Different studies showed malignant transformation rates of 4.12%[11] and 11.4%[17] after laser treatment. Malignant transformation was not observed in our study. This difference in our observation from the previous reports could be due to the short follow-up/recall period and limited sample size. The maximum follow-up/recall period in our study was 2 years and 1 month, while in other studies, the average duration for malignant transformation was 5 years and 9 months.[11] Thus, a long follow-up period and large sample size are required for future studies. The short follow-up period is the primary limitation of our study.

In this study, minor scarring was observed in 5/77 (6.49%) lesions. Scarring was noticed in laser excision rather than laser ablation possibly due to deeper involvement. Pyogenic granuloma-type lesion was seen in one patient after laser excision involving the lateral border/sides of the tongue, which subsided after 10–15 days. The findings were in line with the previous study.[19,20] The current study showed mild-to-moderate post-operative pain (VAS) score after laser treatment. The cases with laser excision experience more pain compared to those in the laser ablation group. Minimal postoperative pain following laser surgery could be due to reduced damage on the nerve endings of the adjacent tissues at high temperatures. Furthermore, the sealed small lymph vessels decrease post-operative pain and oedema.

The results of our study were in accordance with the studies performed by Kharadi *et al*.,[20] Reddy Kundoor *et al*.,[21] Praveen *et al*.,[22,23] Ramwala[24] and Chaudhri *et al*.[25] These studies concluded that the diode laser provides clinical improvement with minimal side effects and thus can be considered one of the best treatment modalities for leukoplakia. These studies are summarised in Table 4.

When comparing the diode laser with other lasers in the management of leukoplakia, diode laser seems to have significantly lesser postoperative pain than CO_2 laser over 2 weeks[16] and better bleeding control and patient satisfaction than Er, Cr: YSGG laser.[26] Very few studies are available, focused on the comparison of diode laser with other lasers in the management of leukoplakia; thus, the author recommends future studies in this aspect.

Laser excision or laser ablation?

This study summarised the guidelines and comparison [Figure 3 and Table 5] to choose between laser ablation and laser excision. These proposed guidelines were based on our experience and the literature.[10,11]

Limitation of the study

The limitations of the current study include short follow-up period, limited sample size and inability to perform a biopsy in all cases. These shortcomings could be attributed to the noncooperation and financial constraints of the patient. Nonetheless, we strongly recommend biopsy in all cases. Furthermore, studies with large sample size and a long follow-up period are required in the future.

Conclusion

Our study aimed to analyse the efficacy of diode laser in the management of leukoplakia. In 51 (66.2%) cases, laser ablation was performed, whereas, in 26 (33.8%)

Table 4: Various studies in accordance of the results of our study

Author	Year	Type of study	Sample size	Clinical outcome	Conclusion
Kharadi *et al*.[20]	2015	Original study	10	Out of 10 patients, 8 showed complete disappearance of lesion even after 6-month follow-up	Diode laser can safely and effectively used as a treatment modality for homogeneous leukoplakia, without any complication and without compromising health and function of patients
Reddy Kundoor *et al*.[21]	2015	Original study	5	70% of the case had mild pain while 3 had just moderate pain	Diode lasers provide acceptable clinical improvement of potentially malignant lesions with minimal side effects
Praveen *et al*.[22]	2015	Original study	10	In almost all cases healing was complete within 3-4-week duration	Diode laser may indeed be the best choice in the management of oral leukoplakia
Ramwala *et al*.[24]	2016	Original study	10	Overall healing was good to very good on the 7th day and excellent on the 30th day in all the cases	Diode laser gives good results after ablation of oral leukoplakia with relatively bloodless field, less pain and overall good patient compliance
Natekar *et al*.[16]	2017	Original study	10	Complete disappearance of the lesion with no pain over 2 weeks	Laser therapy offered better clinically significant results than cryotherapy in the management of OL
Chaudhri *et al*.[25]	2019	Case report	1	Complete disappearance of the lesion	Excision of pre-cancerous oral lesions using laser offers comparative advantages over traditional scalpel excision
Yasmeen *et al*.[14]	2019	Original research	15	Complete disappearance of the lesion with mild pain in the 1st week	Diode provides an alternative technique with marked clinical improvement and high degree of patient acceptance
Praveen *et al*.[23]	2021	Original research	15	Complete disappearance of the lesion with mild pain in the 1st week	Owing to the patient's comfort, laser therapy is quite advantageous over cryosurgery

OL: Oral Leukoplakia

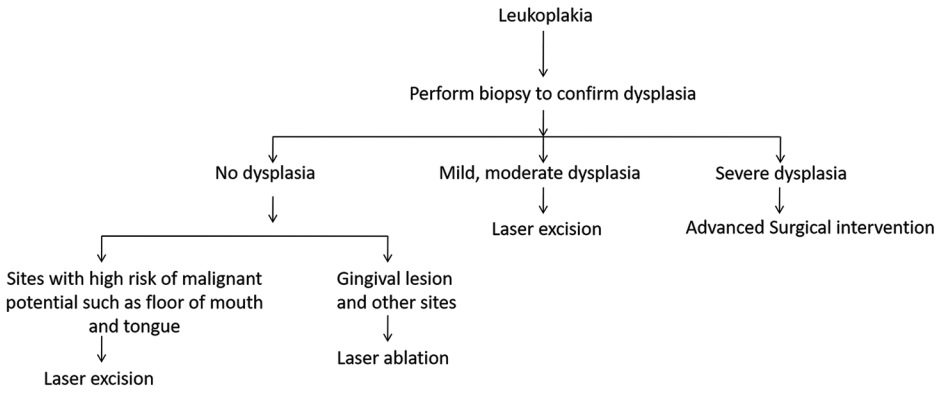

Figure 3: Proposed schematic representation for the guidelines to decide laser excision or laser ablation

Table 5: The comparison between laser ablation and laser excision

Laser ablation/laser evaporation	Laser excision
It is the removal of lesion superficially	It is the removal of lesion deeply, consider an excisional biopsy
Indications	Indications
Leukoplakia without dysplasia	Leukoplakia with dysplasia of any grade
Homogeneous leukoplakia	Non-homogeneous leukoplakia
Large areas where excision could cause discomfort	
Specially indicated in gingival leukoplakia	
Advantages	Advantages
It has limited post-operative discomfort and lesser pain	Tissue removed can be sent for histological examinations
Can be performed in larger lesions	Chances of recurrences are lesser than laser ablation
Can be used in multiple lesions	Difficult for larger lesions
Faster healing	
Reduced scarring and better preservation of tissue's elastic property	
Can be repeated even if new lesions arise near the primary lesion	
Disadvantages	Disadvantages
Tissue cannot be sent for pathological examination. Hence, cannot determine the histology of the lesion	Excising large lesions can cause functional problems
High chances of recurrence	Compared to ablation it has a high chance of tissue scarring

cases, laser excision was performed using diode laser. The recurrence was observed more in the cases managed with laser ablation (25.5%), compared to laser excision (7.6%). Thus, diode laser has proved to be an effective surgical treatment modality for treating leukoplakia. Considering the recurrence rate, laser excision can be considered better than ablation.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

References

1. Warnakulasuriya S, Kujan O, Aguirre-Urizar JM, Bagan JV, González-Moles MÁ, Kerr AR, *et al*. Oral potentially malignant disorders: A consensus report from an international seminar on nomenclature and classification, convened by the WHO Collaborating Centre for Oral Cancer. Oral Dis 2021;27:1862-80.
2. Warnakulasuriya S. Clinical features and presentation of oral potentially malignant disorders. Oral Surg Oral Med Oral Pathol Oral Radiol 2018;125:582-90.
3. Shivhare P, Parihar A. Oral potentially malignant disorder. In: Shivhare P, Parihar A, editors. Textbook of Oral Medicine and Radiology. 2nd ed. Hyderabad: Paras Publisher; 2021. p. 218-58.
4. Swain SK, Debta P. Nonsurgical treatment of oral cavity leukoplakia. Matrix Sci Med 2020;4:91-5.
5. Chen Q, Dan H, Pan W, Jiang L, Zhou Y, Luo X, *et al*. Management of oral leukoplakia: A position paper of the Society of Oral Medicine, Chinese Stomatological Association. Oral Surg Oral Med Oral Pathol Oral Radiol 2021;132:32-43.
6. Grigolato R, Bizzoca ME, Calabrese L, Leuci S, Mignogna MD, Lo Muzio L. Leukoplakia and immunology: New chemoprevention landscapes? Int J Mol Sci 2020;21:6874.
7. Sundberg J, Korytowska M, Holmberg E, Bratel J, Wallström M, Kjellström E, *et al.* Recurrence rates after surgical removal of oral leukoplakia – A prospective longitudinal multi-centre study. PLoS One 2019;14:e0225682.
8. Nammour S, Zeinoun T, Namour A, Vanheusden A, Vescovi P. Evaluation of different laser-supported surgical protocols for the treatment of oral leukoplakia: A long-term follow-up. Photomed Laser Surg 2017;35:629-38.
9. Goharkhay K, Moritz A, Wilder-Smith P, Schoop U, Kluger W, Jakolitsch S, *et al.* Effects on oral soft tissue produced by a diode laser *in vitro*. Lasers Surg Med 1999;25:401-6.
10. Shivhare P, Parihar A. Advanced therapies in oral medicine. In:

Shivhare P, Parihar A, editors. Textbook of Oral Medicine and Radiology. 2nd ed. Hyderabad: Paras Publisher; 2021. p. 858-74.
11. Ishii J, Fujita K, Munemoto S, Komori T. Management of oral leukoplakia by laser surgery: Relation between recurrence and malignant transformation and clinicopathological features. J Clin Laser Med Surg 2004;22:27-33.
12. Sharp MK, Glonti K, Hren D. Online survey about the STROBE statement highlighted diverging views about its content, purpose, and value. J Clin Epidemiol 2020;123:100-6.
13. Deliverska EG, Petkova M. Management of oral leukoplakia – Analysis of the literature. J IMAB 2017;23:1495-504.
14. Yasmeen SA, Reddy BHS, Ramesh MV, Birajdar SS, Yarram A, Kumar NN. Comparative evaluation of diode laser ablation versus scalpel excision for management of oral leukoplakia. J Indian Acad Oral Med Radiol 2019;31:94-9.
15. Tambuwala A, Sangle A, Khan A, Sayed A. Excision of oral leukoplakia by CO2 lasers versus traditional scalpel: A comparative study. J Maxillofac Oral Surg 2014;13:320-7.
16. Natekar M, Raghuveer HP, Rayapati DK, Shobha ES, Prashanth NT, Rangan V*, et al*. A comparative evaluation: Oral leukoplakia surgical management using diode laser, CO2 laser, and cryosurgery. J Clin Exp Dent 2017;9:e779-84.
17. Yang SW, Tsai CN, Lee YS, Chen TA. Treatment outcome of dysplastic oral leukoplakia with carbon dioxide laser – Emphasis on the factors affecting recurrence. J Oral Maxillofac Surg 2011;69:e78-87.
18. de Pauli Paglioni M, Migliorati CA, Schausltz Pereira Faustino I, Linhares Almeida Mariz BA, Oliveira Corrêa Roza AL, Agustin Vargas P, *et al*. Laser excision of oral leukoplakia: Does it affect recurrence and malignant transformation? A systematic review and meta-analysis. Oral Oncol 2020;109:104850.
19. Vivek V, Jayasree RS, Balan A, Sreelatha KT, Gupta AK. Three-year follow-up of oral leukoplakia after neodymium: yttrium aluminum garnet (Nd: YAG) laser surgery. Lasers Med Sci 2008;23:375-9.
20. Kharadi UA, Onkar S, Birangane R, Chaudhari S, Kulkarni A, Chaudhari R. Treatment of oral leukoplakia with diode laser: A pilot study on Indian subjects. Asian Pac J Cancer Prev 2015;16:8383-6.
21. Reddy Kundoor VK, Patimeedi A, Roohi S, Maloth KN, Kesidi S, Masabattula GK. Efficacy of diode laser for the management of potentially malignant disorders. J Lasers Med Sci 2015;6:120-3.
22. Praveen KN, Veeraraghavan G, Reddy S, Kotha P, Koneru J, Yelisetty K. Management of oral leukoplakia using diode laser: A pilot study. BJMMR 2015;10:1-6.
23. Praveen KN, Veeraraghavan G, Ramesh T, Teja TN, Upendra G, Kalyan Y. Efficacy of cryogun versus diode laser therapy in the management of oral leukoplakia. J Indian Acad Oral Med Radiol 2021;33:60-5.
24. Ramwala V. Use of diode laser in the management of oral leukoplakia – A study of 10 cases. IOSR J Dent Med Sci 2016;15:81-5.
25. Chaudhri S, Singh A, Tiwari JD. Oral leukoplakia management using Diode LASER: A case report. J Clin Diagn Res 2019;13:ZD4-6.
26. Sarkar S, Kailasam S, Iyer VH. Effectiveness of diode laser and Er, Cr: YSGG laser in the treatment of oral leukoplakia – A comparative study. Dentistry 2015;5:274.