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ORIGINAL ARTICLE

Three-year follow-up of oral leukoplakia after neodymium: yttrium aluminum garnet (Nd:YAG) laser surgery

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Abstract Oral leukoplakia is a relatively common lesion with a significant proportion of cases changing into cancer. Since most leukoplakias are asymptomatic, the primary objective of treatment must aim at the prevention of such malignant transformation. The main objectives of the study are to observe (1) the efficacy, safety and acceptability of the neodymium:yttrium aluminum garnet (Nd:YAG) laser in the management of oral leukoplakia; (2) the nature of postoperative complications, if any, associated with laser ablation, and (3) the 3-year prognosis of oral leukoplakia treated with laser. Twenty-eight patients with histologically proven leukoplakia were treated with Nd:YAG laser. From this study, we observed that the patients treated with Nd:YAG laser had only mild to moderate pain, swelling and restricted mouth opening, which peaked between 72 h and 1 week. In a majority of the patients the healing was prolonged, to a maximum of 5 weeks, and there was no clinical evidence of scarring in 26 out of 28 cases. In this study we achieved a cure rate of 92.86% in a 6-month period. Further follow-up after 3 years yielded almost the same result, except that one patient was not available for follow-up. We concluded that Nd:YAG laser is an effective device in the management of oral leukoplakia, which is one of the major pre-cancerous lesions in our country.

Keywords Oral lesions · Oral leukoplakia · Nd:YAG laser · Laser surgery · Three-year follow-up

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Introduction

Most invasive oral cancers are preceded by pre-cancerous lesions that can be identified by visual inspection and various invasive and non-invasive diagnostic procedures inside the oral cavity. Oral cancer is, thus, potentially amenable to primary and secondary prevention.

Oral carcinomas often originate as transformations of pre-cancerous mucosal lesions. A pre-cancerous lesion has been defined as a morphologically altered tissue in which cancer is more likely to occur than in its apparently normal counterpart [1]. In developing countries the use of tobacco and/or the areca (betel) nut produces chronic pre-malignant lesions and conditions (leukoplakia, erythroplakia and submucous fibrosis) from which the majority of oral cancers arise. Oral leukoplakia is a very important pre-malignant lesion commonly encountered in India. Oral leukoplakia is considered to be potentially malignant, with a transformation rate ranging form 0% to 20% in 1 to 30 years, according to the type of lesion [2–5]. A 10-year translational study of the oral pre-malignant lesion model suggested that a substantial percentage progress to cancer, especially after treatment has been stopped [6]. In India the incidence of cancerization of oral leukoplakia, one of the most common pre-cancerous diseases, is three-times higher than in western populations [7]. Therefore, proper diagnosis and surgical removal of oral leukoplakia might aid in the

prevention of some oral cancers. Initially, vitamin A, vitamin E and β-carotene were used for the management of leukoplakia. However, because of the limitations, such as the toxicity of vitamin A and the unsatisfactory response to vitamin E and β-carotene, these drugs have been discontinued for the treatment of oral leukoplakia [8–11].

Other modalities suggested for controlling leukoplakia are scalpel excision or electrocautery and cryosurgery. For surgical techniques like scalpel excision, electrocautery, and cryosurgery, there is a recurrence rate of approximately 33% [12, 13]. Moreover, these techniques cause scarring and contraction of large defects, with an added potential of masking any early signs of recurrence if the wound has been sutured or skin graft has been used to cover it [14]. Studies on the clinical usefulness of laser surgery in oral leukoplakia have shown that the management of oral leukoplakia by laser surgery prevents not only recurrence and malignant transformation, but also postoperative dysfunction [15].

Carbon dioxide (CO_2) lasers have been used in a variety of soft tissue surgical procedures, including excision of malignant and leukoplakic lesions in the oral cavity [14, 16]. The neodymium:yttrium aluminum garnet (Nd:YAG) contact laser became available as an alternative to the free-beam CO_2 laser in the mid 1980s. Nd:YAG lasers, due to their deep coagulating capability, are suitable for the management of oral leukoplakia. Laser surgery is associated with little morbidity, low intraoperative and postoperative complication rates, and better disease control than are conventional modes of management. In spite of several worldwide studies of the Nd:YAG laser treatment of oral lesions, few investigations with long-term follow-up have been done in our country [17]. The purpose of the study was to observe (1) the effects of Nd:YAG laser in the treatment of oral leukoplakia, (2) postoperative complications, if any, associated with laser ablation and (3) the prognosis of oral leukoplakia in a three-year period after laser treatment.

Materials and methods

Twenty-eight volunteers (17 male and 11 female) with histologically proven leukoplakia were selected for Nd:YAG laser treatment after informed consent had been obtained. Only patients with no, mild or moderate dysplasia were included for the study. Patients with severe dysplasia were not considered for selection. In the 28 patients dysplasia was present in 15 (nine had mild dysplasia and six had moderate dysplasia). The age of 64% of the patients was above 50 years, of which that of 32% was over 60 years. Only 11% belonged to the age group 30–39 years. A 1,064 nm Nd:YAG laser (Dornier Medilas Fibertom 4060, Dornier, Germany), with a power range of 1–60 W, was used. Laser delivery was through a 400 μm bare fibre, and the power for leukoplakial excision was set at 15 W. The total energy at the site varied, depending on the extent of the lesion. All the laser safety precautions were undertaken during the time of surgery. The surgical intent was to remove the lesion, superficially, with a margin of clinically healthy appearing mucosa, on an out-patient basis, under local anaesthesia, as in the procedure described by Panje et al. [18]. The margins of the lesions were identified clinically; a moat incision was made around the lesion, with a margin of approximately 3 mm. The incision depth was controlled to the level of connective tissue only, visually. The tissue was undermined, with the laser in the contact mode, to peel off the surface. This area was subjected to laser application in non-contact mode for coagulation. The excision sites were allowed to heal by secondary intent. Appropriate postoperative instructions were given. Antibiotics were given to medically compromised patients and to those who developed oedema. Non-steroidal anti-inflammatory drugs (NSAIDs) were prescribed for pain. Postoperative pain was assessed on a 10-point scale, where 0 denoted no pain and 10 denoted severe pain. The patients were followed up at 72 hours, weekly for 5 weeks, monthly for 6 months and yearly follow up for 3 years. The assessment of their pain and swelling for a period of 5 weeks is shown in Fig. 1.

Results and observations

The study included 28 patients with leukoplakia treated with Nd:YAG laser. Of the 28 patients, seven had lesions in the commissure, six in the buccal mucosa, five in the sulcus/vestibule/gingiva, and ten had lesions on the tongue.

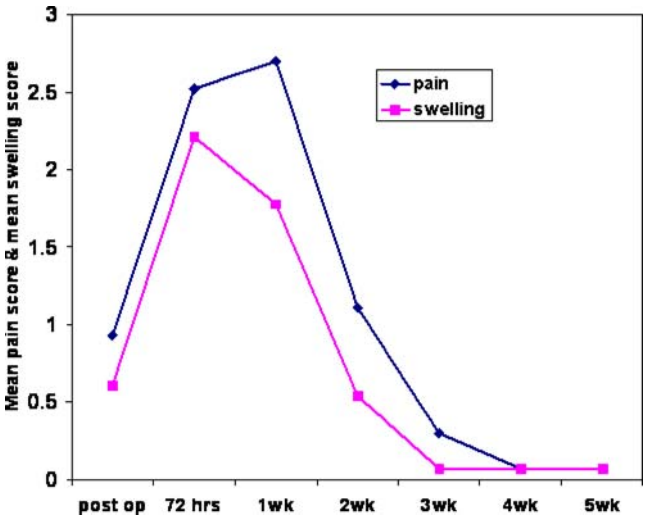

Fig. 1 Assessment of pain and swelling up to a period of 5 weeks

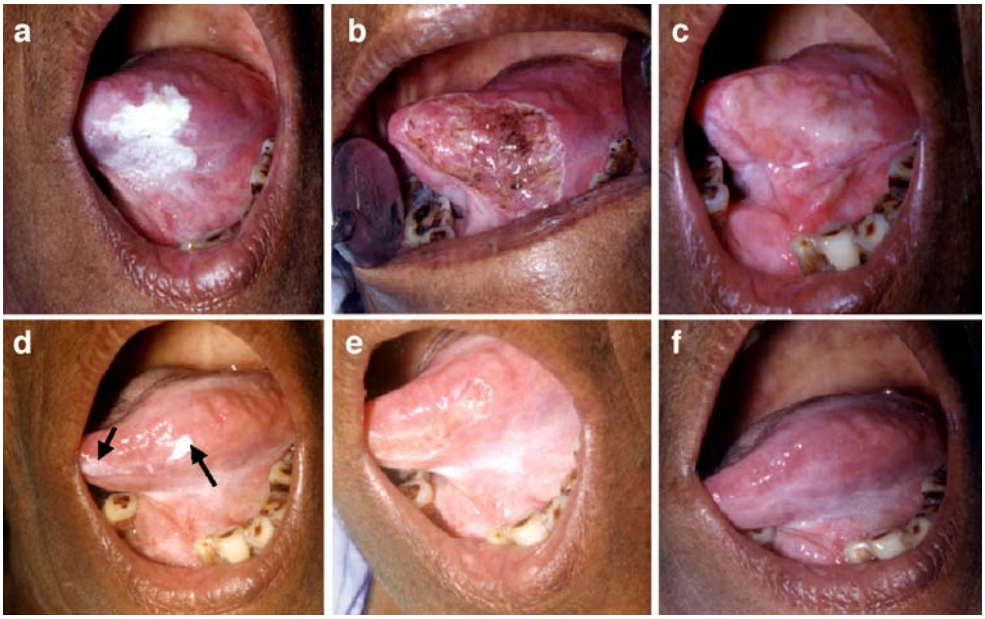

Fig. 2 A case of recurrence treated with a second session of laser. **a** Leukoplakia on the tongue, before the first treatment. **b** Immediate postoperative view. **c** Two weeks after laser resection. **d** Sites of recurrence (*arrows*). **e** After the second application of laser. **f** At 3-year follow-up

Of the patients, 54% had lesions exhibiting dysplasia (22% moderate, 32% mild). All our patients had to be given NSAIDs, and 50% were prescribed antibiotics. During postoperative assessment, invariably in all patients the treated area was the same colour as the connective tissue. After 72 h, all the sites became yellow. In 1 week 18% of cases were yellow and red at the treated area. At 2 weeks, all except one had become yellow and red. At 3 weeks 57% continued to be yellow and red, 25% were red and 11% became pink/normal. At 5 weeks, only one (3.5%) remained yellow and red, one (3.5%) became red, and 26 (93%) exhibited normal mucosa at the site of laser application. There were two recurrences; both were treated by a second application of laser (Fig. 2). We could achieve complete control in only one of the re-treated cases, whereas, in the other, the lesion recurred. During the follow-up period two of our patients who had oral submucous fibrosis (OSMF) developed squamous cell carcinoma at a different site in the oral cavity. However, in both these patients, the site of laser ablation remained normal during the follow-up period of 6 months. There was one incidence of carcinoma development adjacent to the site of laser application. Of the 28 patients treated, only two (7.15%) developed infection 72 h after the procedure, and, by 1 week the number became three. All wounds were infection free by the 2nd week (Figs. 3 and 4). The

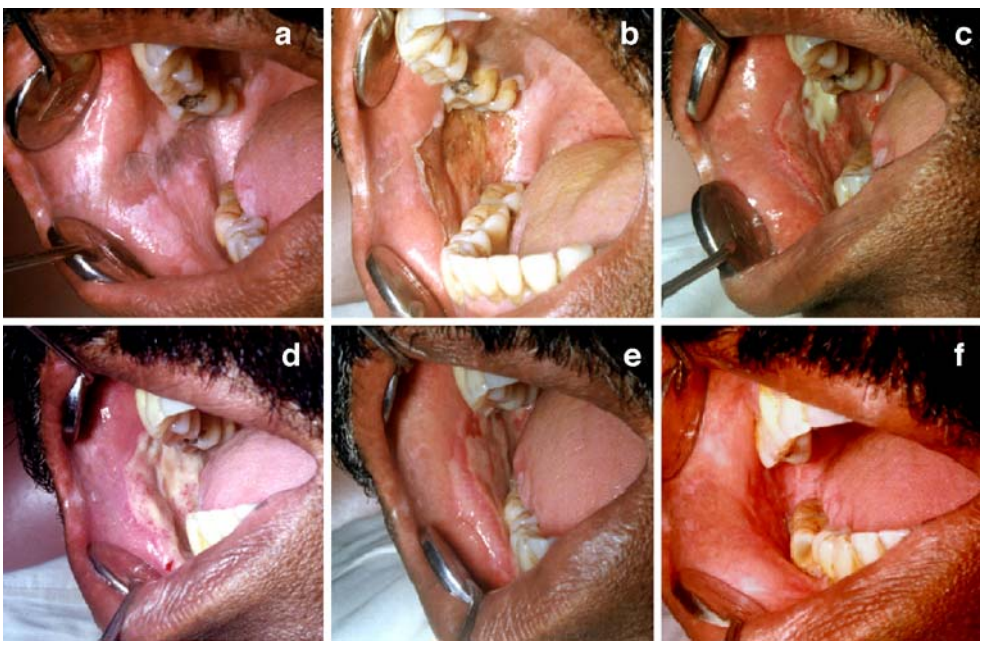

Fig. 3 All stages of leukoplakia of the right buccal mucosa treated with Nd:YAG laser. **a** Before treatment. **b** Immediately after treatment. **c** After 72 h. **d** After 1 week. **e** After 3 weeks. **f** At the 3-year follow-up

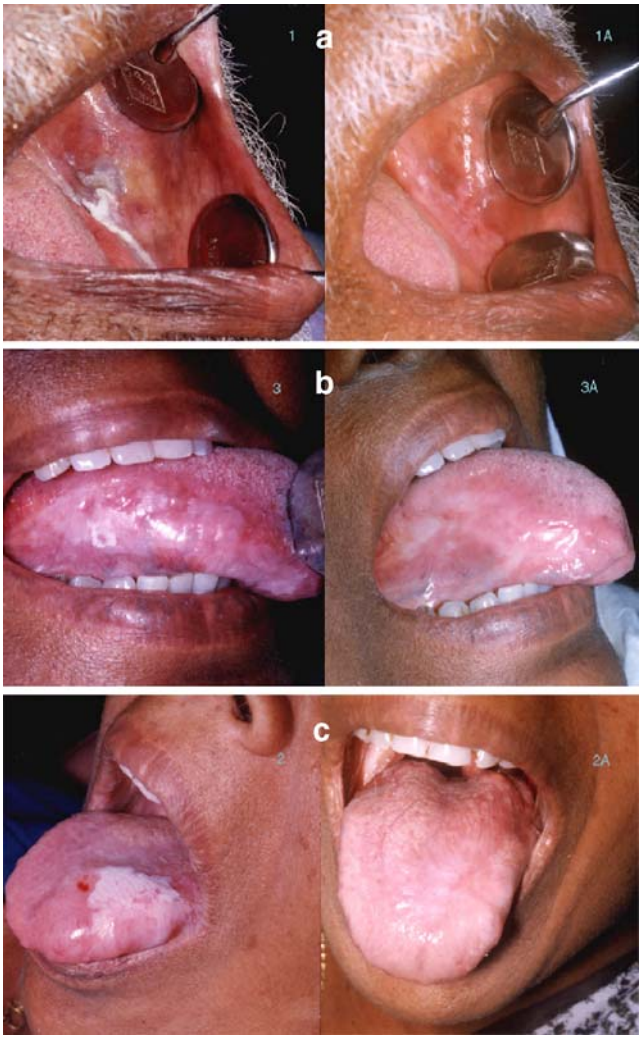

Fig. 4 Pre-treatment and 3-year follow-up of Nd:YAG laser-treated leukoplakia at different sites. **a** Left buccal mucosa and retro-molar area. **b** Dorsum and left side of the tongue. **c** Right lateral border of the tongue

assessment of pain and swelling are summarized in Fig. 1. The result after 6 months is summarized in Table 1. Yearly follow-up was carried out for 3 years. During this period, one patient was not available for follow-up (Table 2).

Table 1 Results after 6 months

Parameter	Number	Remarks
Total cases	28	
Complications		
1. Granuloma	1	On the tongue—resolved itself
2. Carcinoma	3	In OSMF patients. 2—different site, 1—at adjacent site
Recurrence	2	Including carcinoma at adjacent site
Treatment successful	**26**	Cure rate **92.86%**

Table 2 Results after 3 years

Parameter	Number	Remarks
Total cases	28	
Complications		
1. Granuloma	1	On the tongue—resolved itself
2. Carcinoma	3	In OSMF patients. 2—different site, 1—at adjacent site
Recurrence	3	1 recurrence 1 adjacent-site carcinoma 1 lost to follow-up
Treatment successful	**25**	Cure rate after 3 years **89.28%**

Discussion

In our study we evaluated the effects of Nd:YAG laser for the treatment of 28 patients with oral leukoplakia. Some authors, such as White et al. and Schoelch et al., have reported success in the treatment of oral leukoplakia, using Nd: YAG laser [19, 20]. We adopted the Nd:YAG laser for our patients due to (1) its availability, (2) the convenience of application, (3) the possibility of treatment on an out-patient (OP)basis under local Anaesthesia, (4) the ability for large areas to be treated in a single application, and (5) the possibility of precise control of laser energy in areas where access was difficult. Observing the clinical events following treatment, we found that there was a threefold increase in swelling at 72 h, after which it had become minimal by the end of the 1st week. This pattern was in accordance with those observed by White et al. and Schoelch et al. [19, 20]. All our patients complained of pain, which could be managed by common NSAIDs, mostly between 72 h and 1 week, after which time the pain started to reduce and had become minimal by 2 weeks. Patients with treated tongue lesions reported pain on a higher scale. This pattern of pain following laser surgery is in accordance with studies by some authors [19, 20] but disagrees with the findings of Roodenburg et al. [21]. Even though restriction of mouth opening was noted in some patients, it was not statistically significant. Moreover, its pattern followed that of pain; hence, it was attributed to pain rather than trismus. In all comparable studies 20–40 W laser energy was used, but, in our study, we could achieve excellent results with 15 W Nd:YAG laser energy. In most of our patients complete healing was seen in 5 weeks. Healing by 3 weeks, as claimed by some authors [19, 20], was observed only in three cases (11%), where the lesion area was < 170 mm^2. Three of our patients who developed oral cancer (two at a different site and one at an adjacent site) had underlying OSMF and hence it was attributed to the same, as OSMF

has a high rate of malignant transformation [22]. As previously reported by Chu et al. [14], one of our patients developed a granuloma on the dorsum of the tongue, which resolved itself. All the 26 cases healed without scarring. In this study we achieved a cure rate of 92.86% in a 6-month period (Table 1). Further follow-up after 3 years yielded almost the same result, except that one patient was lost to follow-up. We had to include this finding as a treatment failure/recurrence, taking into account the worst possibility. This brought the cure rate down to 89.28% (Table 2). Our study is in consistence with the findings of Ishii et al. that laser excision is suitable for leukoplakia on the tongue and buccal mucosa [15].

Conclusion

In the study we found that the Nd:YAG laser had the advantage of precise delivery of laser through fibre-optic cable. The surgical sites showed excellent wound healing, with no scarring and minimal postoperative pain. The cure rate of 89.28% (25/28 patients) after 3 years is much better than that of other surgical treatment modalities. Absence of complications, such as bleeding, paresthesia or anaesthesia, very low recurrence rates and excellent healing make laser treatment superior to other methods of treating oral leukoplakia. The Nd:YAG laser is, thus, an effective device in the treatment of oral leukoplakia.

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