Recurrence of Premalignant Lesions of the Oral Cavity and Oropharynx after Initial Treatment with Pulsed Diode Laser Excision

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Introduction

- Leukoplakic mucosal lesions of the oral cavity and oropharynx have a 1% incidence in the population and may harbor preneoplastic changes of hyperkeratosis or dysplasia
- Maximizing local control of premalignancies while limiting pain, bleeding, tethering, and functional deficits including dysphagia, trismus, and dysarthria is challenging
- There is a medical need for low morbidity, tolerable therapies which mitigate progression of disease in early stages [1,2]
- Pulsed diode lasers (PDLs) have a remarkable affinity for water-based tissue, providing both precision and coagulation for excision of superficial lesions with little damage to deeper tissue [3] and there have been few studies evaluating the use of PDLs in treatment of oral and oropharynx leukoplakia
- Recurrence rates after PDL treatment have previously been reported as 8 – 38% for oral cavity hyperkeratosis and 19.5 % for oral cavity mild-moderate dysplasia [4, 5, 6]
- Malignant transformation of oral cavity hyperkeratosis and mild-moderate dysplasia have previously been reported as 2.6 - 9 % and 10.4% after PDL, respectively [5,6]

Objective: To assess the recurrence of oral cavity and oropharyngeal hyperkeratosis and mild dysplasia after initial treatment with pulsed diode laser excision.

Methods

- Retrospective review of patients at an academic institution between 2013 and 2020
- **Inclusion Criteria:**
  - Patients with oral cavity or oropharyngeal hyperkeratotic or mild dysplastic lesions treated at least once with PDL
  - Each distinct leukoplakic or dysplastic lesion were recorded as separate entries even if present in the same patient
- **Exclusion Criteria:**
  - Lesions treated with CO_2 laser or another laser other than PDL
  - Lesions pathologically diagnosed as malignancy
- **PDL Settings:**
  - 5 watts on super pulsed mode
- **Main Outcome Measure:**
  - Recurrence of oral cavity or oropharyngeal hyperkeratosis or mild dysplasia after each PDL excision
- **Other Variables:**
  - Smoking history, number of laser treatments, laser settings, site and size of lesion, pathology, history of previous surgery or excisional biopsy at the lesion site, transformation of pre-cancerous hyperkeratosis or mild dysplasia lesion to malignancy

Results

- Total patients: 14; Total lesions: 18

Table 1: *Patient Characteristics*

Patient Characteristics (N = 14)	Proportion
Female	9 (64.3%)
Age at first PDL treatment	66.6 years (range, 46-85)
Average BMI	25.5 (range, 17.9-41.1)
Smoking status	
Never smoker	7 (50%)
Former smoker	4 (28.6%)
Current smoker	3 (21.4%)

Table 2: *Lesion Characteristics*

Lesion Characteristics (N = 18)	Proportion
Pathology	
Hyperkeratosis	9 (50.0%)
Mild dysplasia	4 (22.2%)
Hyperkeratosis and mild dysplasia	5(27.8%)
Site	
Oral cavity	17 (94.4%)
Oropharynx	1 (5.6%)
Subsite	
Oral Tongue	11 (61.1%)
Buccal Mucosa	4 (22.2%)
Hard palate	2 (11.1%)
Soft palate	1 (5.6%)
Location of PDL treatment	
Operating Room	7 (38.9%)
Clinic	8 (44.4%)
Operating Room and Clinic	3 (16.7%)
Mean time from clinical diagnosis to first PDL treatment	8.3 months (range, 0-44)
Average number of PDL treatments per lesion	1.4 (range, 1-4)
Recurrence after final PDL excision	16.7%*
Average time between PDL treatment and any recurrence	20.6 months (range, 0-81)
Average follow up time after recent PDL	27.8 months (range, 2-87)

**Patients did not receive subsequent PDL treatment due to lack of follow up.*

Discussion

- None of the lesions underwent malignant transformation
- *Complications of Treatment:*
  - One patient developed pyogenic granuloma and reported chronic tongue pain
  - This patient was treated with PDL in the OR

Table 3: *Hazard Ratios for Predictors of Lesion Recurrence*

	Hazard Ratio (95% CI)	Significance (p< 0.05)
Only 1 PDL Treatment	0.365 (0.024~5.526) ↓	.467
Diagnosis of Hyperkeratosis	0.288 (0.025~3.292) ↓	.317
Diagnosis of Mild Dysplasia	2.591 (0.233~28.855) ↑	.439
Age First PDL Treatment	0.990 (0.906~1.082) ↓	.822
Time from Diagnosis to PDL Treatment	1.092 (1.001~1.191) ↑	.048 *
PDL in Clinic	1016955483.113 (0.000~∞) ↑	.999
PDL in Operating Room	0.216 (0.018~2.635) ↓	.230

* *Time from diagnosis to first PDL treatment demonstrated a significantly higher hazard ratio for the event of lesion recurrence.*

Conclusion

- In this series, PDL treatment of hyperkeratosis and mild dysplasia showed low complication rates and reasonable control of these precancerous lesions in both the clinic and in operating room settings
- None of the patients in this series experienced excess bleeding, tethering, or dysarthria after PDL treatment
- A longer time from diagnosis to first PDL treatment resulted in a significant higher hazard of recurrence, demonstrating the importance of early intervention with PDL treatment
- PDL may be considered as a safe and effective treatment for hyperkeratosis and mild dysplasia of the oral cavity and oropharynx, but further study is warranted

References

1. Bettendorf O, Piffko J, Bankfalvi A. Prognostic and predictive factors in oral squamous cell cancer: important tools for planning individual therapy? Oral Oncol. 2004;40(2):110–9.
2. Scheifele C, Reichart PA. Oral leukoplakia in manifest squamous epithelial carcinoma. A clinical prospective study of 101 patients. Mund Kiefer Gesichtschir. 1998;2(6):326–30.
3. Gutiérrez-Corrales, A et al. "Comparison of diode laser - Oral tissue interaction to different wavelengths. In vitro study of porcine periodontal pockets and oral mucosa." *Medicina oral, patologia oral y cirugia bucal* vol. 25,2 e224-e232. 1 Mar. 2020, doi:10.4317/medoral.23317
4. 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 Feb;22(1):27-33. doi: 10.1089/104454704773660949. PMID: 15117484.
5. Sundberg J, Korytowska M, Holmberg E, Bratel J, Wallstro¨m M, Kjellstro¨m E, et al. (2019) Recurrence rates after surgical removal of oral leukoplakia—A prospective longitudinal multicentre study. PLoS ONE 14(12): e0225682. https://doi.org/10.1371/journal.pone.0225682
6. Jerjes W, Upile T, Hamdoon Z, Al-Khawalde M, Morcos M, Mosse CA, Hopper C. CO_2 laser of oral dysplasia: clinicopathological features of recurrence and malignant transformation. Lasers Med Sci. 2012 Jan;27(1):169-79. doi: 10.1007/s10103-011-0916-z. Epub 2011 Apr 15. PMID: 21494890.