Impact of CO2 Laser and Scalpel Excision on Intraoperative Bleeding, Postoperative Pain and Scarring following excision of Oral Leukoplakia – A Systematic Review

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ABSTRACT

Oral Leukoplakia is defined as, "a predominantly white lesion of the oral mucosa that can't be characterized as any other definable lesion; some oral leukoplakias will transform into cancers." Treatment and management of patients with oral precancerous lesions are determined by evaluating their risk for malignant progression which is 1.5% to 34% for oral leukoplakic lesions. It is crucial that clinicians embrace the importance of early detection and treatment of premalignant lesions. Surgical removal with cold-blade scalpel excision or electrocautery excision significantly reduces the risk of transformation of the lesion. Laser surgery has shown to exhibit several advantages over scalpel for many procedures. This study sought to determine if there was a difference in the intensity of pain, hemostasis and rate of wound healing/ or scar formation following excision with scalpel when compared to excision done with a CO2 laser.

Keywords: Oral leukoplakia, CO2 laser, Scalpel Excision, Intraoperative Bleeding, Postoperative pain, Scarring.

INTRODUCTION

Leukoplakia, a primarily white oral mucosal lesion, has recently been defined as a distinct entity that cannot be classified as any other defining lesion [1]. It poses a significant concern as some oral leukoplakias have the potential to transform into malignancies. The etiological factors associated with leukoplakia include alcohol consumption, smoking, oral tobacco use, and recent trauma (from teeth) [1]. Unfortunately, the majority of oral leukoplakias are not curable, emphasizing the importance of early detection and prevention. Individuals with leukoplakia face a significantly elevated risk of developing oral cancer, estimated to be 50-60 times greater than that of the general population [2]. Furthermore, leukoplakia exhibits a gender and age predilection, primarily affecting men and commonly diagnosed during the fifth and sixth decades of life. Globally, the predicted prevalence of leukoplakia ranges from 2% to 3% [3], with an annual incidence rate of 1.1 to 2.4 per 1000 male patients and 0.2 to 1.3 per 1000 female patients [4]. Understanding the epidemiological characteristics and risk factors associated with leukoplakia is crucial for effective management and prevention strategies.Three clinical subtypes of nonhomogeneous leukoplakia are recognised:[5]

1. Speckled leukoplakia
2. Nodular leukoplakia
3. Verrucous leukoplakia

Oral leukoplakic lesions exhibit varying rates of malignant transformation, with an overall range of 1.5% to 34%. When considering homogeneous lesions, the transformation rate is approximately 3%, whereas nonhomogeneous lesions have a wider range of 13.4% to 14.5%

[6]. Additionally, erosive lesions demonstrate a 28% likelihood of developing malignant transformation, whereas verrucous leukoplakia has a transformation rate of 4.6% [6].

The progression of proliferative verrucous leukoplakia (PVL) involves the transition from flat patches to exophytic and verrucous lesions [7]. Even after undergoing ablative therapy, PVL exhibits a recurrence rate of up to 85% [8]. Consequently, close monitoring of PVL patients is essential. Distinguishing between inflammatory lesions and genuine leukoplakia is facilitated by a comprehensive clinical history. Various mucosal injuries, such as frictional keratoses, morsicatio, linea alba, thermal and chemical mucosal burns, among others, can mimic leukoplakic lesions. By carefully assessing the location and conducting thorough patient interviews, a diagnosis of mucosal injury can be established [8].

Several risk factors have been identified in relation to the development of oral leukoplakia such as tobacco, smokeless tobacco, alcohol, actinic damage, submucous oral fibrosis, human papilloma virus and Qihanhui Shang.[5,9-17]

Recognizing and treating premalignant lesions at the earliest possible stage is of utmost importance in oral healthcare. A clinical examination combined with a biopsy serves as the gold standard for identifying and diagnosing oral premalignant lesions. In addition to these traditional methods, several complementary tools have flooded the market, offering alternative means of lesion detection. These tools include autofluorescence, vital staining, and brush cytology/biopsy.

Treatment becomes necessary for high-risk lesions and those exhibiting moderate to severe dysplasia upon biopsy evaluation. To ensure effective management, complete removal of all affected epithelium associated with the oral precancerous lesion is required.[4] This approach significantly reduces the risk of the lesion undergoing changes during surgical removal, as seen with procedures involving a cold-blade scalpel or electrocautery excision.

Another viable treatment option for oral premalignant lesions is laser ablation, with the CO2 laser being the most commonly employed. The damaged epithelium is typically vaporized using the precise and targeted energy of the CO2 laser. Notably, the CO2 laser's ability to close small blood arteries contributes to minimal bleeding during surgery and improved visibility.

As a result, the CO2 laser has gained significant favor among oral surgeons for treating pathologic diseases of the oral mucosa. Due to its affinity for water-based tissues, the CO2 laser has emerged as the most well-established laser for excisional biopsies of the oral mucosa. Its versatility extends to the treatment of early-stage benign lesions, premalignant lesions, and oral cancers.[18]

The aim of this study is to evaluate and compare the impact of using the CO2 laser and scalpel in managing intraoperative bleeding, postoperative pain, and scarring following the excision of oral leukoplakia. By examining these outcomes, we aim to provide valuable insights into the effectiveness and benefits of these treatment modalities in the management of oral premalignant lesions.

MATERIALS AND METHODS

This systematic review was reported according to the Preferred Reporting Items for Systematic Reviews and the protocol was registered in the International Prospective Register of Systematic Reviews database (**CRD42023397715).**

The PICO strategy was as follows:

(1) Patients: Patients were diagnosed with OL confirmed through clinical manifestations and a histological examination

(2) Intervention: OL lesions were vaporized or excised by CO2 laser.

(3) Control: Traditional scalpel excision for management of oral leukoplakia.

(4) Outcome: Pain, hemostasis and scarring following surgical excision.

(5) Study design: Included studies were randomized controlled studies, retrospective cohorts, case-control studies, and prospective investigations.

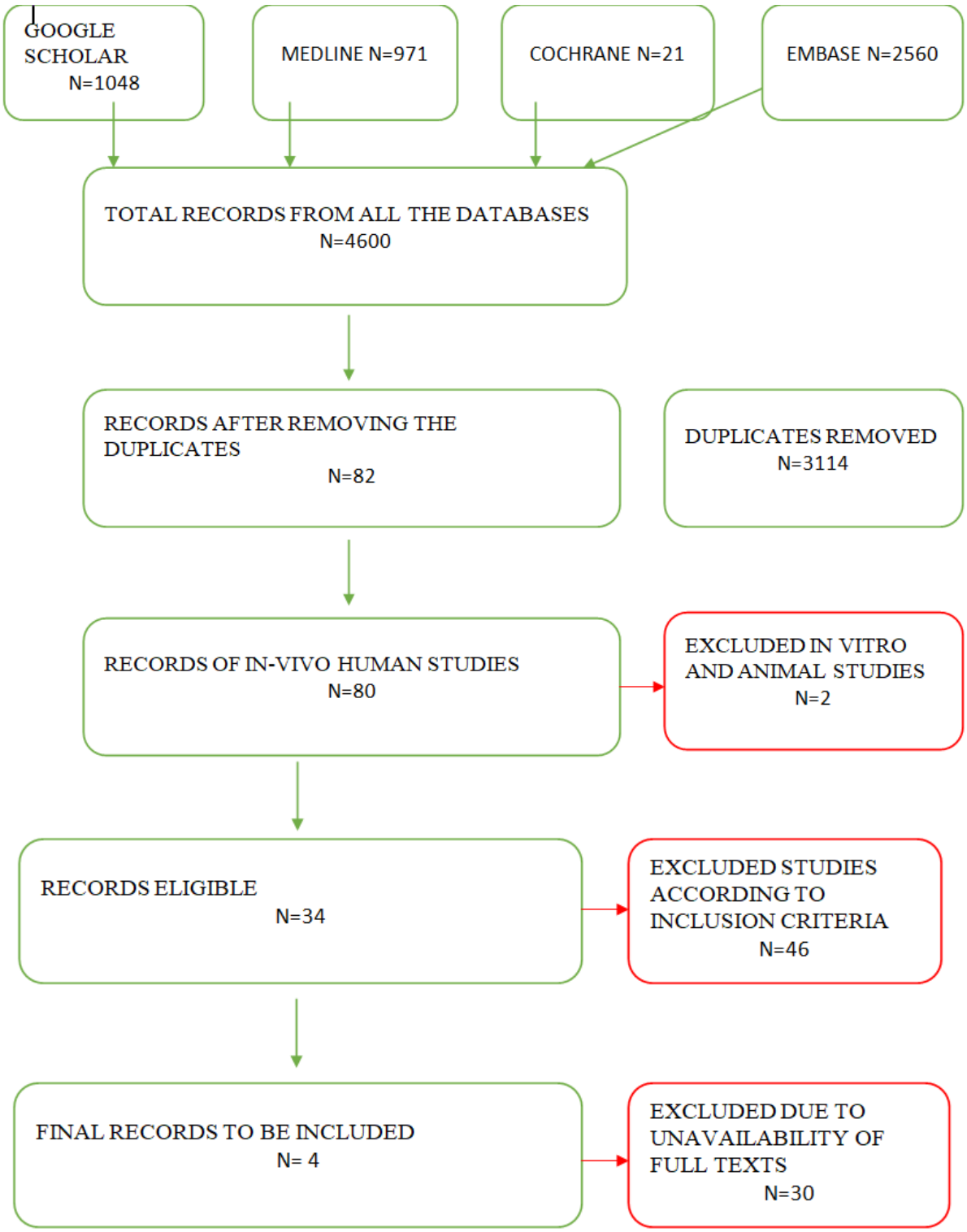
The inclusion criteria for the study encompassed specific requirements to ensure the relevance and reliability of the data. These criteria were as follows:

- Patients between the ages of 20 and 60 years were included in the study. This age range was chosen to focus on adult patients who are more likely to present with leukoplakia and undergo excision procedures.
- The study included patients who had been diagnosed with leukoplakia and had undergone excision using either a scalpel or a CO2 laser. By including patients who underwent excision procedures, the study aimed to evaluate the impact of these treatment modalities on intraoperative bleeding, postoperative pain, and scarring.
- A minimum follow-up period of at least two weeks was required for the included patients. This follow-up period allowed for the assessment of postoperative outcomes and any potential complications that may arise during the healing process.
- The study specifically included presentations in the English language. This criterion was implemented to ensure consistency in data extraction and analysis, as well as to facilitate the understanding and dissemination of the study findings.
- Studies published between January 1980 and December 2022 were considered for inclusion in the study. This time frame was chosen to encompass a wide range of relevant literature and ensure the inclusion of recent advancements in the field of oral leukoplakia management.

The study implemented exclusion criteria to ensure the focus and reliability of the data analysis. The exclusion criteria were as follows:

a) Non-randomized controlled trials, book chapters, personal opinions, letters, conference abstracts, qualitative studies, duplicate studies, experimental lab studies, case studies, reviews, systematic reviews, observational studies, and animal studies were excluded from the analysis. By excluding these types of studies, the study aimed to prioritize high-quality and controlled research designs for a more rigorous analysis.
b) Studies involving patients younger than 20 years or older than 60 years were excluded from the study. This age range restriction aimed to focus on the adult population and maintain consistency within the selected patient group.
c) Studies published in languages other than English were excluded. This criterion was implemented to ensure uniformity in data extraction and analysis, as well as to overcome language barriers for the research team.
d) Articles that only provided abstracts without full-text access were excluded from the study. This criterion aimed to ensure that the selected studies provided sufficient information for comprehensive analysis.
e) Studies in which the CO2 laser was compared with treatment modalities other than the scalpel were excluded. This criterion aimed to maintain a specific focus on the comparison between the CO2 laser and the scalpel as treatment options, allowing for a more targeted analysis of their respective impacts.

SEARCH STRATEGY



STUDY SELECTION

The criteria for considering studies for this review were randomized controlled trials (RCTs) that evaluated the effects of CO2 laser and/or scalpel in the management of oral leukoplakia lesions.

RESULTS

The following data of included studies analysed and summarized in **Tables 1,2,3,4,5**

TABLE 1: STUDY CHARACTERISTICS

Sr No	Author Name (Year Of Study)	Journal Name	Study Design	Conducted Accordance With	Approval Of Protocol
1.	Aruna Tambuwala	J. Maxillofac. Oral Surg. DOI 10.1007/s12663-013-0519-2	COMPARATIVE RCT	NS	NS
2.	Sunil vasudev	*Journal of Advanced Clinical & Research Insights* (2016), 3, 147–151	Prospective	NS	NS
3.	Tousiffaridsyed	Journal of Lasers in Medical Sciences Volume 3 Number 1 Winter 2012	Retrospective	NS	NS
4.	Pia lopezjornet	Med Oral Patol Oral Cir Bucal. 2013 Jan 1;18 (1):e38-44.	RCT	NS	The Ethics Committee of the University of Murcia.

TABLE 2: PARTICIPANT CHARACTERISTICS

Sr No	Geogra Phic Area	Participa Nt Population	Total No.	Mean Age (Years)	Site
1.	**India**	Thirty patients with bilateral (60 Lesions) were selected for the entire proposed research.	**30 (BILATERAL)**	15-70yrs	(60 lesions right and Left buccal mucosa)
2.	**India**	A total of 23 patients with oral leukoplakia were included in this study;	**23 (32-72 yrs)**	23	The most common site of the lesion was predominantly in the buccal mucosa in 12 patients followed by commissures in 5 patients, tongue in 3 patients, and vestibule in 3 patients
3.	**India**	8 patients who were	**8**	44/M	Right and Left buccal

		diagnosed with prominent features of OL			mucosa
6	**Spain**	48 patients (27 males and 21 females) with a mean age of 53.7 ± 11.7 years and diagnosed with oral leukoplakia	**48**	53.7 ± 11.7 years	10 in cheek mucosa (20.8%), 24 in gums (50%), 8 in palate (16.8%), 3 in tongue (6.2%) and 3 in floor of the mouth (6.2%).

TABLE 3: METHODOLOGICAL CHARACTERISTICS OF STUDIES

Sr No	Study	Experimental interventions (CO2 Laser)	Control interventions (Scalpel)	Follow up(Months)
1	**Aruna Tambuwala**	Carbon dioxide laser unit-Union medical model no: UM-L25, 2012 with an input voltage of 220 V/50 Hz and Power consumption of 500 W classified as class I, b type (size 940 9 400 9 400 mm).	Scalpel and BP blade no 15	**Pain = post op day 1 and 2 bleeding= intraop scarring= 1 month swelling=**
2	**Sunil vasudev**	Surgical CO2 laser unit with power output between 0.5 and 15 W and focal length of 12.5 cm	NA	**10.4 months**
3	**Tousiffarids yed**	Left side- CO2 laser with power density adjusted	Right side- removed with scalpel	**1,2,3 week**
4	**Pia lopezjornet**	(20)(10 males and 10 females) was treated by CO2 laser (Lasersat 20W, Satelec®, Pierre Rolland, SATELEC®, S.A., Barcelona, Spain).	Cold knife (28)	27.90 ± 12.05 months

TABLE 4: MAIN OUTCOMES OF STUDY

Sr no.	Study	Pain	Hemostasis	Wound healing
1.	Aruna Tambuwala	VAS SCALE 1st post-op day (mean SD) Laser2.20 (0.41) scalpel2.36 (0.49) p value 0.212 2nd post-op day (mean SD)Laser 1.24 (0.44) Scalpel 1.32 (0.48) P value 0.533	By gauze pieces laser-1.5 scalpel 4.5	Vancouver scar assessment scale Scarring after 1 month (after 1 month) (mean SD) laser1.52 (0.68)Scalpel 1.95 (0.69) p value 0.045
2.	Sunil vasudev	21 patients did not need to use analgesics beyond the prescribed 5-day	NS	3-6 weeks

		period, and those who used beyond the 5-day period had lesions >4 cm.		
3.	Tousiffaridsyed	Faces and NRS scale laser 1st say 0-8 scalpel 6-8 7th day 0-2 and scalpel 0-3	NS	NS
4.	Pia Lopez Jornet	VAS Pain and swelling reported by the patients was greater with the cold knife than with the CO2 laser, with statistically significant differences between the two techniques during the first three days after surgery (p-value for related samples at 12h, 1, 2 and 3 days ≤ 0.05). Followed by a gradual decrease over one week in both groups	NS	NS but SWELLING given

TABLE 5: RISK OF BIAS ASSESSMENT FOR INCLUDED STUDIES

Sr.No.	**Author Andyear Ofstudy**	**Risk Of Bias Assessment**					**Overall Assessment**
		DOMAIN 1	**DOMAIN 2**	**DOMAIN 3**	**DOMAIN 4**	**DOMAIN 5**	
1.	**Aruna Tambuwala**	LOW	SOME CONCERNS	LOW	SOME CONCERNS	SOME CONCERNS	SOME CONCERNS
2.	**Sunil vasudev**	LOW	LOW	LOW	HIGH	LOW	High
3.	**Tousiffaridsyed**	SOME CONCERNS	HIGH	SOME CONCERNS	LOW	LOW	High
4.	**Pia lopezJornet**	Some concerns	Low	low	Low	Some concerns	low

DISCUSSION

The premalignant lesion known as leukoplakia is thought to be frequent in the mouth. There are several different treatment plans for oral leukoplakia, including surgical ones like excision, medicinal ones like retinoids and vitamin A, and cryotherapy laser therapies. [19] The best results for CO2 laser surgical therapy of oral leukoplakia (lesion confined to epithelium or sub mucosa) come from ablation or vaporisation of the lesion. When performing ablation in a defocused mode (achieved by moving the laser away from the tissue and beyond its focal length), the laser beam's power and depth of penetration are reduced (200–400 lm per pass), limiting the destruction to the epithelium and resulting in less discomfort, swelling, and even scarring with a better return of the tissue's elastic properties.

The use of CO2 lasers has certain serious drawbacks. Of particular concern are the risks of radiant radiation exposure to the patients, surgeon, and surgical team that could result in laser skin burns, eye damage, and blindness. Additional drawbacks include the high cost of laser equipment and servicing costs, the requirement for further training of the operating team and surgeon, and ongoing maintenance and technology advancement. One must take into account additional aspects, such as patient costs and health risks, when evaluating the treatment of an oral soft tissue lesion.

In a split-mouth procedure, compared the excision of leukoplakia in the buccal mucosa using a CO2 laser and a scalpel.[7] Their study population included 30 patients (M>F) who each had 60 identical bilateral leukoplakic lesions. Between the ages of 22 and 70, 68% of the population smoked cigarettes daily for more than five years, and 88% chewed tobacco. On the first and second postoperative days, the author noticed that the scalpel caused more bleeding, and there was no discernible pain difference between the two techniques. Compared to scalpels, which took between 3-6 minutes, CO2 lasers took between 6 and 10 minutes. Lesions removed using a laser had far less blood loss than those removed with a scalpel, allowing for better intraoperative hemostasis.[20]. Van de Hem et [21] observed that patients with the most extensive lesions (2 cm) displayed higher postoperative pain, and they advised the vaporisation in several sessions for patients with extensive lesions after surgically treating 282 oral leukoplakias (in 200 patients) with CO2 laser.

Other factors that are important to patients include reduced pain and a low likelihood of post-interventional problems. All of these clinical factors were assessed in the current investigation. Only studies that compare the clinical results of a scalpel and a CO2 laser or an Er:YAG laser are included in the literature. [3] All three, they found, are suitable for excisional biopsies. The CO2 laser is the best tool for excisional biopsies if haemostasis is required. Based on the results of the current investigation, a surgical safety distance of 0.2 mm for the Er:YAG laser and of 0.5–1 mm for the CO2 laser is recommended in comparison to the scalpel to prevent a compromised histological examination.

Sloughing was evident on the second day following cryosurgery, however it was not present when the patient was checked one week after the procedure. Slough, which might function as a physical barrier delaying wound healing, was seen in the early days. Better wound healing, reduced contraction, less scarring were the outcomes of laser surgery. Scar formation, which was observed in individuals who underwent cryosurgery, was completely absent in groups who underwent laser surgery. Nonetheless, this scar (after cryosurgery) settled and vanished six months after the operation.[8]

Despite the fact that all three surgical methods studied in this study were successful in treating leukoplakia, the results of the study showed that CO2 and diode lasers were superior in terms of minimising pain intensity, infection, and scar formation. Diode laser therapy outperformed CO2 laser therapy in terms of pain relief. No recurrence was discovered in any of the three trial groups during a 6-month follow-up. The cryosurgery group had the longest follow-up at 24 months, followed by the CO2 laser group at 18 months, and the diode laser group at 12 months.

CONCLUSION

Based on the findings from the studies included in this analysis, it has been established that the utilization of CO2 laser in the management of oral leukoplakia is highly effective and exhibits superiority over traditional scalpel excision. The evidence suggests that CO2 laser treatment results in reduced pain levels, minimal intraoperative bleeding, faster healing, and absence of postoperative scarring, thereby offering distinct advantages. However, it is important to acknowledge that scalpel excision remains the current gold standard. To further strengthen the available evidence and minimize bias, it is recommended to conduct new

randomized controlled trials (RCTs) with larger sample sizes, longer follow-up periods, and comprehensive outcome measures. Such studies will contribute to generating robust evidence regarding the effectiveness of CO2 lasers in the management of oral leukoplakia.

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