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Evaluation of the Effectiveness of the Carbon Dioxide (CO2) Laser in Minor Oral Surgery: A Systematic Review

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Abstract

Introduction: Lasers in oral surgery have been extensively studied in recent years. Laser treatment is now a well-known technology that is frequently employed on oral soft tissues. The carbon dioxide (CO2) laser was one of the first soft tissue removal lasers. Because of the strong affinity of the CO2 laser to water, it is best used for removing, vaporizing, and coagulating these tissues. In minor oral surgery, CO2 laser therapy has shown advantages. Therefore, this study examined the CO2 laser use in minor oral soft tissue surgery.

Methods: The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) standards were followed in this study. A question for research encompassing the inclusion criteria for the participants, intervention, comparison, outcome, and study design (PICOS) was formulated. The search queries were entered into the PubMed/Medline, Scopus, and Embase databases. Consideration was given to publications published between January 1, 2018 and March 15, 2023.

Results: The research included 37 studies after narrowing search results, eliminating duplicate titles, and conducting an eligibility review (three animal studies, seven case reports, three case series, and twenty-four clinical studies). CO2 lasers alone or in combination with other therapies successfully treated oral potentially malignant disorders (OPMDs), oral tumors, oral fibrous-epithelial lesions, gingival melanin hyperpigmentation, pyogenic granuloma, socket preservation, mucocele, high labial frenulum attachment, and so on. CO2 lasers reduced intra- and postoperative complications and adverse effects, improved postoperative functional results, ablated tissues with precision, and minimized disease recurrence and malignant transformation.

Conclusion: Our study found that the CO2 laser in oral minor surgeries is successful, but further randomized clinical trials and multicenter studies are recommended to compare CO2 laser surgery to other treatments.

keywords: CO2 laser; Oral surgery; Oral soft tissue lesions; Laser surgery; Oral mucosa.

Introduction

"Laser" is the scientific term for light amplification by stimulated emission of radiation.[1] An essential active medium, the source of atoms, is required for the production of a radiation-stimulated light source. The active medium, which recognizes and classifies the kind of laser beam emitted, might be a material that is liquid, solid, or gas.[2]

Laser treatment is now a well-known technology that is frequently employed on a variety of oral surfaces, including soft, hard, and tooth tissues.[3] The utilization of a laser in the oral cavity depends on many aspects such as the wavelength of the laser beam, the desired depth of radiation penetration into the various tissues, the interaction duration (pulsed or continuous laser), the pulse repetition rate, radiation power, energy, energy density, regions exposed to radiation, and the pulse length.[4]

Lasers with different intensities are utilized for distinct purposes in dentistry. Low-intensity lasers (Ga-As, As-Ga-Al, etc) can detect cavities, treat pain, address neuromuscular diseases, reduce inflammation, and speed healing. High-intensity lasers like Nd:YAG, Er:YAG, and carbon dioxide (CO2) are utilized in surgical procedures such as the excision or incision of soft tissues as well as the removal of dental calculus and cavities.[5,6]

High-intensity lasers cut and remove lesions from soft tissue by absorbing light, producing heat, drying, coagulating, vaporizing, or charring. Radiation causes three zones—vaporized, necrotic, and coagulated—over healthy tissue.[5,7] Several studies have shown that soft tissue surgery in dentistry may be performed using lasers.[8-11]

Laser therapy reduces scarring, edema, bleeding, bacteremia, and postoperative discomfort, and it has better cut control and precision, without a need for sutures.[11] For oral soft tissue surgery, Er:YAG, Nd:YAG, CO2, and diode lasers are the most common lasers.[11] The

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oral soft tissue vascularization, pigmentation, and water content should be considered when selecting a laser.[6]

One of the earliest lasers used in soft tissue surgery was the CO2 laser. This laser was authorized for this usage in 1976 and has been utilized for oral tissue surgery since 1970.[8] The CO2 laser may operate in continuous or pulsed modes, and it produces light with wavelengths of 10 600 nm and 9300 nm. It is utilized in a number of oral surgery, such as frenectomy, gingivectomy, treatment of ulcers (aphthous), and gingival re-epithelialization of periodontal therapy. Due to the high temperature of the laser beam, the properties of the CO2 laser enable strong hemostasis of tiny blood vessels, quick and effective tissue removal, preservation of sterility, and a reduction in initial inflammatory responses and discomfort after surgery (because of the sealing of sensory nerve terminals). Oral tissues, which contain between 70% and 90% water, are among the water-rich tissues that the CO2 laser vaporizes due to its high water absorption efficiency. Thus, it is best used for removing, vaporizing, and coagulating these tissues.[6, 9-11] Once intracellular water absorbs CO2 laser energy, cellular rupture results from the photothermal impact. The ability of the CO2 laser to perform surgery is based on cellular vaporization.[12]

As a result of the wavelength ability to penetrate soft tissue and quickly generate heat that is subsequently transferred to the tissue around it, a very small area (approximately 500 μm) of thermal necrosis is produced.[13] Because of this impact, compared to alternative methods of incision, hemostasis and lymphatic closure, which are clinical manifestations of the coagulation of vessels, have been shown to reduce postoperative bacteremia. Reducing lateral thermal damage in a tiny region is an important benefit of CO2 laser usage.[14]

The advantages of employing CO2 laser treatment in minor oral surgery have been reported in specific instances; however, these claims have not been evaluated. Moreover, documented techniques that might be used in other investigations and in clinical practice are required. Also, there has not been much research done comparing the efficacy of CO2 laser treatment to other forms of treatment. Thus, the current study aimed to evaluate the effectiveness of the CO2 laser in minor oral surgery by reviewing previous studies on this subject. Practitioners and researchers interested in the use of lasers in oral surgery will gain information from our review and could use our data to improve their treatments.

Material and Methods

Protocol

Our systematic review followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.[15] Prior to beginning the review, a question for research encompassing the inclusion criteria for the participants, intervention, comparison, outcome, and study design (PICOS) was formulated and is displayed in Table 1.

Information Sources and Search Strategy

Table 2 shows the outcomes of a comprehensive electronic search of three sources (PubMed/Medline, Scopus, and Embase). Articles published between January 1, 2018 and March 15, 2023 were taken into consideration. For probable inclusion in the research, an additional manual search was undertaken on the bibliographies of the articles that were retrieved, as well as on the bibliographies of other relevant published systematic and narrative reviews.

Eligibility Criteria

Our review evaluated only published studies pertinent to our PICOS query (Table 1). Our review excluded non-English studies due to the study team's language competency.

Study Selection

The titles and abstracts of the items found via the literature search were evaluated by two separate reviewers (MBR and MSS). After completing the screening procedure, the

Table 1. Eligibility Criteria for the Present Systematic Review

Domain	Inclusion Criteria	Exclusion criteria
Participants	– Patients, lesions and conditions that require minor surgery in the oral cavity, such as oral leukoplakia, oral lichen planus, gingival hyperpigmentation, Fordyce granule removal, oral premalignant lesion, mucocele, ranula, pyogenic granuloma, gingival hyperplasia, *Epulis fissuratum*, lymphangioma, hemangioma, oral cancers, oral biopsy, oral vascular malformations, tooth extraction, endodontic surgery, frenectomy and ankyloglossia.	Surgery in parts other than oral cavity and oral major surgeries
Intervention	– The application of the CO2 laser alone or in combination with other methods in oral surgery in forms of vaporization, coagulation and ablation.	Nonsurgical usage of the CO2 laser in oral cavity
Comparison	– Other procedures or not taking therapy at all	–
Outcome	– Outcomes that measure the effectiveness of CO2 laser surgery, such as bleeding, wound healing, pain, recurrence rate and other postoperative complications.	Studies which used the CO2 laser in oral minor surgery, but there was not information about post-operative problems
Study design	– Prospective/retrospective clinical trials, animal studies, ex-vivo studies, in-vitro studies, case reports, case series, and none-comparative studies	Systematic reviews with or without meta-analysis, narrative reviews, short communications, and letters to the editors

Table 2. Strategies for Database Searches, From 2018 up to March 15, 2023

Database	Search Strategy	Hits
Medline	((((("mouth mucosa"[MeSH Terms] OR ("mouth"[All Fields] AND "mucosa"[All Fields]) OR "mouth mucosa"[All Fields] OR ("oral"[All Fields] AND "mucosa"[All Fields]) OR "oral mucosa"[All Fields]) AND ("lesion"[All Fields] OR "lesion s"[All Fields] OR "lesional"[All Fields] OR "lesions"[All Fields])) OR (("gingiva"[MeSH Terms] OR "gingiva"[All Fields] OR "gingival"[All Fields] OR "gingivally"[All Fields] OR "gingivals"[All Fields] OR "gingivitis"[MeSH Terms] OR "gingivitis"[All Fields] OR "gingivitides"[All Fields]) AND ("hyperpigmentated"[All Fields] OR "hyperpigmentation"[MeSH Terms] OR "hyperpigmentation"[All Fields] OR "hyperpigmentations"[All Fields] OR "hyperpigmention"[All Fields])) OR (("fordyce"[All Fields] OR "fordyce s"[All Fields]) AND ("cytoplasmic granules"[MeSH Terms] OR ("cytoplasmic"[All Fields] AND "granules"[All Fields]) OR "cytoplasmic granules"[All Fields] OR "granule"[All Fields] OR "granulate"[All Fields] OR "granulated"[All Fields] OR "granulates"[All Fields] OR "granulating"[All Fields] OR "granulation"[All Fields] OR "granulations"[All Fields] OR "granulative"[All Fields] OR "granulator"[All Fields] OR "granulators"[All Fields] OR "granule s"[All Fields] OR "granules"[All Fields] OR "granulous"[All Fields])) OR (("mouth"[MeSH Terms] OR "mouth"[All Fields] OR "oral"[All Fields]) AND ("dysplasia"[All Fields] OR "dysplasias"[All Fields])) OR (("mouth"[MeSH Terms] OR "mouth"[All Fields] OR "oral"[All Fields]) AND ("precancerous conditions"[MeSH Terms] OR ("precancerous"[All Fields] AND "conditions"[All Fields]) OR "precancerous conditions"[All Fields] OR "premalignant"[All Fields] OR "premalign"[All Fields] OR "premalignancies"[All Fields] OR "premalignancy"[All Fields]) AND ("lesion"[All Fields] OR "lesion s"[All Fields] OR "lesional"[All Fields] OR "lesions"[All Fields])) OR (("mouth"[MeSH Terms] OR "mouth"[All Fields] OR "oral"[All Fields]) AND ("melanoma"[MeSH Terms] OR "melanoma"[All Fields] OR "melanomas"[All Fields] OR "melanoma s"[All Fields])) OR (("mouth"[MeSH Terms] OR "mouth"[All Fields] OR "oral"[All Fields]) AND ("biopsie"[All Fields] OR "biopsy"[MeSH Terms] OR "biopsy"[All Fields] OR "biopsied"[All Fields] OR "biopsies"[All Fields] OR "biopsy s"[All Fields] OR "biopsying"[All Fields] OR "biopsys"[All Fields] OR "pathology"[MeSH Subheading] OR "pathology"[All Fields])) OR "leukoplakia, oral"[MeSH Terms] OR "lichen planus, oral"[MeSH Terms] OR (("mouth"[MeSH Terms] OR "mouth"[All Fields] OR "oral"[All Fields]) AND ("vascular malformations"[MeSH Terms] OR ("vascular"[All Fields] AND "malformations"[All Fields]) OR "vascular malformations"[All Fields])) OR (("endodontal"[All Fields] OR "endodontic"[All Fields] OR "endodontical"[All Fields] OR "endodontically"[All Fields] OR "endodontics"[MeSH Terms] OR "endodontics"[All Fields]) AND ("surgery"[MeSH Subheading] OR "surgery"[All Fields] OR "surgical procedures, operative"[MeSH Terms] OR ("surgical"[All Fields] AND "procedures"[All Fields] AND "operative"[All Fields]) OR "operative surgical procedures"[All Fields] OR "general surgery"[MeSH Terms] OR ("general"[All Fields] AND "surgery"[All Fields]) OR "general surgery"[All Fields] OR "surgery s"[All Fields] OR "surgerys"[All Fields] OR "surgeries"[All Fields])) OR "frenectomy"[All Fields] OR "Fiberotomy"[All Fields] OR "Mucocele"[MeSH Terms] OR "Ranula"[MeSH Terms] OR "granuloma, pyogenic"[MeSH Terms] OR "Gingival Hyperplasia"[MeSH Terms] OR "Lymphangioma"[MeSH Terms] OR "Tooth Extraction"[MeSH Terms] OR "Hemangioma"[MeSH Terms] OR "Mouth Neoplasms"[MeSH Terms] OR "Bisphosphonate-Associated Osteonecrosis of the Jaw"[MeSH Terms] OR "Ankyloglossia"[MeSH Terms] OR ("surgery, oral"[MeSH Terms] OR "Oral Surgical Procedures"[MeSH Terms])) AND "co2 laser"[All Fields]) AND (2018:2023[pdat])	49
Scopus	ALL ("oral mucosa lesions" OR "Oral leukoplakia" OR "Oral lichen planus" OR "gingival hyperpigmentation" OR "Fordyce granule" OR "Oral dysplasia" OR "Oral melanoma" OR "oral premalignant lesion" OR "Mucocele" OR "Ranula" OR "Pyogenic granuloma" OR "Gingival hyperplasia" OR "Epulis fissuratum" OR "Lymphangioma" OR "Hemangioma" OR "oral cancer" OR "oral biopsy" OR "Oral vascular Malformations" OR "Bisphosphonate-associated osteonecrosis of the jaws" OR "tooth extraction" OR "Endodontic surgery" OR "Frenectomy" OR "Fiberotomy" OR "Ankyloglossia" OR "oral squamous cell carcinoma" OR "oral surgery" OR "Oral Surgical Procedures " AND "CO2 laser") AND PUBYEAR > 2017 AND PUBYEAR < 2017	363
Embase	('oral mucosa lesions' OR 'oral leukoplakia' OR 'oral lichen planus' OR 'gingival hyperpigmentation' OR 'fordyce granule' OR 'oral dysplasia' OR 'oral melanoma' OR 'oral premalignant lesion' OR 'mucocele' OR 'ranula' OR 'pyogenic granuloma' OR 'gingival hyperplasia' OR 'epulis fissuratum' OR 'lymphangioma' OR 'hemangioma' OR 'oral cancer' OR 'oral biopsy' OR 'oral vascular malformations' OR 'bisphosphonate-associated osteonecrosis of the jaws' OR 'tooth extraction' OR 'endodontic surgery' OR 'frenectomy' OR 'fiberotomy' OR 'ankyloglossia' OR 'oral squamous cell carcinoma' OR 'oral surgery' OR 'oral surgical procedures') AND 'co2 laser' AND [2018-2023]/py	41

two reviewers evaluated the full-text versions of possibly admissible research and determined the final article selection. The third author (MA) arbitrated disputes amongst the reviewers. Eventually, for data extraction and analysis, publications that met the inclusion criteria were included.

Data Extraction

From the chosen papers, two reviewers (MBR and MSS) retrieved the following information:

1- Study characteristics, such as the authors and the publication year

2- Study type and sample

3- The condition or lesion for laser treatment

4- CO2 laser parameters (wavelength, emission mode, average power, spot size, and the focus type)

5-Comparison

6- The findings of the study

Quality and Risk of Bias

According to the modified instructions of the Consolidated Standards of Reporting Trials (CONSORT) statement, the risk of bias among RCTs was disclosed. Using the Cochrane Handbook for Systematic Reviews of Interventions, the risk of bias for each study was calculated.[16]

Sections including randomization and allocation concealment, blinding of patients and examiners with outcome assessment, completion of trials by all patients with withdrawals, and selective reporting were considered. The overall quality of the studies was classified as "low risk of bias", "high risk of bias" or "unclear" for each of the section mentioned above.[17]

Results

Study Selection

In total, the primary search approach came up with 453 articles: 363 from Scopus, 49 from PubMed/Medline, and 41 from Embase. After removing duplicates, 401 abstracts were left for title and abstract assessment. 340 publications were omitted because of incompatibility with our search criteria, leaving 61 articles for final full-text evaluation. Eventually, 37 article studies were chosen

for comprehensive analysis after adding 2 articles via reference screening, and their main information was imported to tables. Figure 1 shows the flow diagram of the systematic review.

Study Characteristics

Three animal studies, seven case reports, three case series, and twenty-four clinical trials made up the 37 included studies (Table 3). The selected studies were categorized as follows: oral potentially malignant disorders (OPMDs) (n = 12), soft tissue tumors (n = 10), wound healing after tooth extraction (n = 2), gingival hyperpigmentation (n = 3), pyogenic granuloma (n = 2), mucocele (n = 3), and other conditions such as fibrous hyperplasia, trigeminal neuralgia, and pemphigus. Table 3 displays the descriptive features of the studies.

Result of Individual Studies

Oral Potentially Malignant Disorders

OPMDs are premalignant lesions of the oral mucosa. Leukoplakia, lichenoid dysplasia, lichen planus, and actinic cheilitis are the most frequent OPMDs.[55,56]

Twelve studies evaluated CO2 laser surgery in OPMDs. Oral tumors and OPMDs were found in three studies.[24-26] Some studies showed no postoperative complications [20,42,43] ,and one study found no complication in 64.1% of the patients,[18] whereas others claimed the following complications:

- Postoperative pain: In a research study,[23] the numerical rating scale (NRS) score declined considerably from 1 month to 1 year. In additional trials, visual analog scale (VAS) ratings varied from 2 to 4,[44] 0 after 7 days,[25] 1.8 on the first day before declining to 0.03 on day 7,[26] and 6 in 10.4% of the patients.[19] Another study reported pain in 28.2% of the lesions.[18] Another study revealed 20% of the subjects felt pain on day 4.[22]
- Recurrence rates in studies were: 54.17 %,[19] 52.6% after a mean of 4.8 years,[18] 44.0% after a mean of 19.7 months,[21] 35.1%,[20] 20% after 1 month,[22] 13.63 %,[25] 9.1%,[23,42] and 3.3% with a nodal recurrence.[26]
- Malignant transfor mation (MT) was different from no MT after 1 year,[23] 2% MT at 18 months of the study,[19] 2.27%,[42] 2.6% MT after 174 and 26 months of the study,[18] 4% during the 48th month of the study,[21]

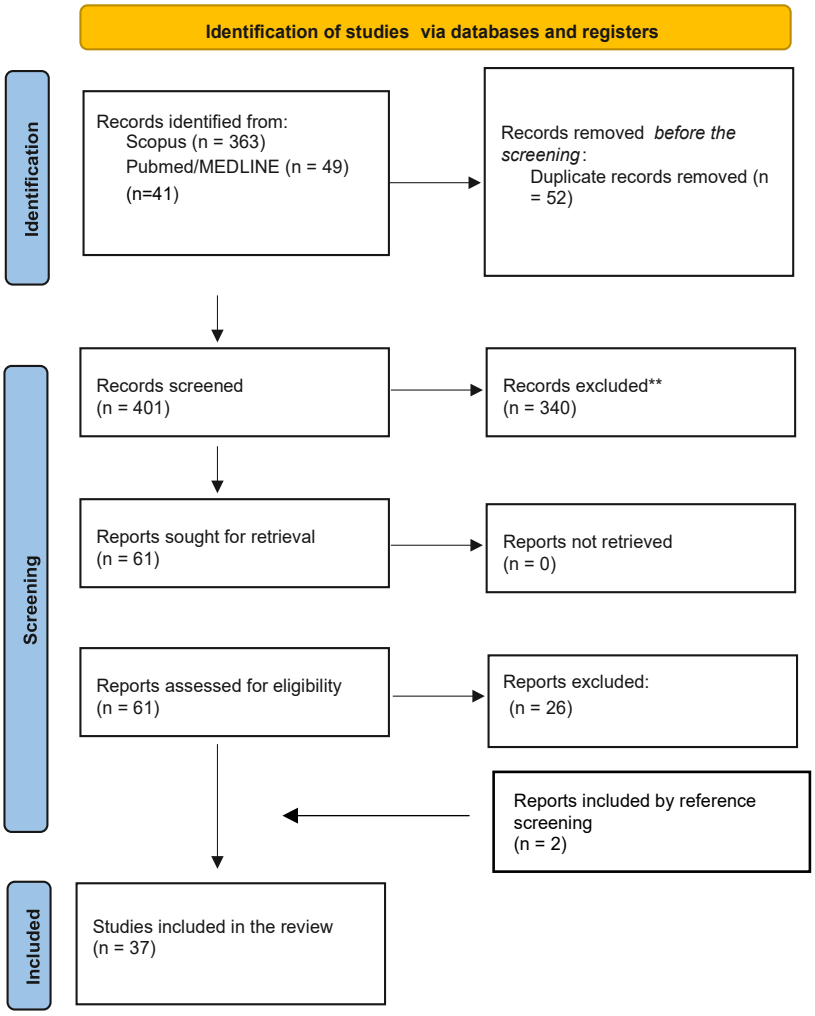

Figure 1. Flow Diagram of the Systematic Review

Table 3. A Summary of Studies Utilizing the CO2 Laser in Minor Oral Surgery

First Author and year	Type of Study	Sample	The condition/lesion for using laser	Laser CO2 characteristics					comparison	Result of study
				wavelength	Emission mode	Average power	Spot diameter at the focus	Focus-to-tissue		
Vilar-Villanueva, 2022[18]	Clinical study	58 patients	Oral leukoplakia	-	Continuous or pulsed	3-12 W	-	-	None	Only the margin showed a substantial correlation with the recurrence of lesions after vaporization.
Rodriguez-Lujan, 2022[19]	Clinical study	34 patients	Oral leukoplakia	-	Continuous mode	5-10 W	-	-	None	The treatment success rate was 43.75%. No significant differences between studied variables were found with regard to recurrence.
Campos, 2022[20]	Clinical study	37 patients	Oral leukoplakia	10600 nm	Continuous mode	5-10 W	-	-	None	The CO2 laser was efficient but the clinical result of malignancy or recurrence was not avoided.
Cloitre, 2018[21]	Clinical study	25 patients	PVL, leukoplakia, lichen planus, actinic cheilitis, and lichenoid dysplasia	10966 nm	-	10-20w	-	-	None	The annual recurrence rate and malignant transformation rate were 18.3% and 1.7%. OPMDs managed by the CO2 laser had a significant recurrence rate, especially in those with hyperplasia.
Gupta, 2021[22]	Clinical study	20 patients	Oral leukoplakia	10600 nm	Continuous mode	2 W	0.44 mm	-	Diode laser	The CO2 laser had less thermal collateral damage, pain, erythema, swelling, burning, and recurrence than the diode laser.
Matsumoto, 2019[23]	Clinical study	16 patients (9 had laser therapy)	Oral lichen planus	10600 nm	Continuous mode	3 W	-	defocused	none	The(TS) and NRS scores dropped dramatically from one month to one year after treatment.
Rosenthal, 2021[24]	Clinical study	62 patients	OPMDs T1 cancers and benign tumors	-	-	15 W	-	-	Electrocautery	On day 7, electrocautery produced greater pain than the CO2 laser and the pain ratings of the laser group dropped faster. Also, a tendency toward improved quality of life, quicker return to regular diet, and return to work in the CO2 laser was noted. However, these results were not statistically significant
Saibene, 2019[25]	Clinical study	78 patients	PVL, lichen planus papilloma leukoplakia venous arteriosus malformation, cistoadenoma, pseudo-fibroma, mucocele, leukoerythroplakia	-	continuous and pulsed mode	4 and 6 W	-	-	None	No patients had intraoperative issues. All procedures (removals, exeretic biopsies, and vaporizations) were effective. No negative laser-related lesion responses were noted.
Thomas, 2018[26]	Clinical study	30 patients	Leukoplakia, erythroplakia, squamous cell carcinoma	-	pulsed or continuous mode	5-15 W	-	-	None	CO2 had quick re-epithelization, softer scar, little intraoperative bleeding, postoperative functional impairment and pain, and no oncological impact.
Gardenal, 2022 [27]	Clinical study	81 patients	Oral and oropharyngeal cancers	-	Super pulsed mode	3-10 W	-	-	None	The first surgery resected 81.5% of the tumors. The average post-operative pain was manageable with medications, and saliva, taste, and speech were satisfactory. The lowest ratings were for shoulder and chewing problems.
Toledano-Serrabona ,2019[28]	Clinical study	36 patients	Oral squamous cell papilloma	-	continuous mode	3-5 W	0.8 mm	focusd	Er,Cr:YSGG laser & scalpel	Recurrence rates across groups did not vary.

Table 3. Continued.

First Author and year	Type of Study	Sample	The condition/lesion for using laser	Laser CO2 characteristics					comparison	Result of study
				wavelength	Emission mode	Average power	Spot diameter at the focus	Focus-to-tissue		
Luna-Ortiz, 2019[29]	Clinical study	20 patients	Squamous cell carcinoma, oral mucosal melanoma, myofibroblastic sarcoma, mucoepidermoid carcinoma, synovial sarcoma, pleomorphic adenoma, adenoid cystic carcinoma	-	-	-	-	-	none	For the treatment of minor lesions in the oral cavity, the CO2 laser is a suitable surgical approach.
Tenore, 2019[30]	Clinical study	10 patients	carcinoma in situ, peripheral giant cell granuloma, mucocele, granular cell tumor, kaposiform hemangioendothelioma, focal fibrous hyperplasia	10600 nm	Super pulse wave	4.2 W	0.2-0.4 mm	Focused mode	none	All specimens' surgical resection margins were thermally affected by the CO2 laser, but histological analysis was unaffected.
Nammour, 2021[31]	Clinical study	781 patients	Benign oral squamous papilloma	10600 nm	continuous wave	3-4 W	0.3 mm	focused	Scalpel & Diode laser & ND:YAG laser	In terms of recurrence, there was no discernible difference between laser wavelengths and scalpel.
Nammour, 2020[32]	Clinical study	143 patients	Venous malformation, capillary hemangioma, and venous lake	10600 nm	continuous wave	1 W	-	defocused	Nd:YAG laser & Diode laser & Er,Cr:YSSG laser	Unlike the diode and Nd:YAG groups, the vascular lesions treated with CO2 and Er,Cr:YSGG lasers did not recur after one year. There was no discernible difference in the cosmetic result reported by patients and practitioners at the conclusion of the six-month follow-up.
Monteiro, 2019[33]	Clinical study	130 patients	Fibromas, fibro-epithelial hyperplasias, fibropapillomas, and denture-related fibrous hyperplasias	10600 nm	-	4 W	0.5 mm	Focused mode	electrosurgical scalpel, cold scalpel Diode laser, Er:YAG laser, and Nd:YAG laser	Diode had the highest epithelial score, followed by Nd:YAG, electric scalpel, CO2, Er:YAG, and cold scalpel, and the highest connective score was electric scalpel followed by CO2, diode, Nd:YAG, Er:YAG and cold scalpel. The electrosurgical scalpel caused the most tissue damage, followed by diode, Nd:YAG, CO2, Er:YAG, and cold scalpel. Using a cold scalpel as a comparison, the CO2 laser group had the most regular incision.
Suter, 2019[34]	Clinical study	75 patients	Fibrous hyperplasia	10600 nm	Char free mode	4.62 W	0.2 mm	-	scalpel and Er:YAG laser	The duration of intervention, intraoperative bleeding, and swelling with the CO2 laser is less than the Er:YAG laser and scalpel. Pain and analgesic use were similar among groups and Er:YAG had a less thermal damage region than CO2.
Nammour, 2020[35]	Clinical study	72 patients	Gingival melanin hyperpigmentation	10600 nm	super pulsed mode	1.5 W	-	-	Diode & Er:YAG	The longest-lasting stability in therapy is offered by the diode laser. The Er:YAG laser results in the quickest time before gingival pigmentation reappears.
Tran, 2022[36]	Clinical study	38 patients	Gingival melanin hyperpigmentation	10600 nm	continuous mode	2.5 w	-	-	None	Patients who received CO2 laser treatment reported less pain and complete epithelization after one week. The Dummett–Gupta Oral Pigmentation Index (DOPI) indices for CO2-laser-treated sites considerably decreased after four weeks.

Table 3. Continued.

First Author and year	Type of Study	Sample	The condition/lesion for using laser	Laser CO2 characteristics					comparison	Result of study
				wavelength	Emission mode	Average power	Spot diameter at the focus	Focus-to-tissue		
Moeintghavi, 2022[37]	Clinical study	12 patients	Gingival melanin depigmentation	10600 nm	continuous wave	3 W	1 mm	focused	Diode laser	During the 6-month follow-up, the diode laser had a superior esthetic result than the CO2 laser. Both lasers demonstrated equivalent color change across treatment phases and similar bleeding and VAS pain ratings.
Liu, 2020[38]	Clinical study	20 patients	Pyogenic granuloma	10600 nm	ultrapulsed	2~3 W	-	focused	none	The combination of Nd: YAG laser and CO2 laser therapy healed all patients. All patients were satisfied with no scar after wound healing and recurrence at 12-months
Kazakova, 2018[39]	Clinical study	18 patients	Gingivectomy	10600 nm	continuous wave	9.69 W	2.5 mm	focused	surgical scalpel, Er:YAG laser, ceramic bur, Electro-cautery and diode laser	A thin coagulation layer, limited microscopic breakage, and strong blood coagulation were all visible with the CO2 laser and it was the best instrument that had excellent results.
Sfasciotti, 2020[40]	Clinical study	26 patients	High labial frenulum attachment	10600 nm	Super pulse wave	4.5 W	-	-	Diode laser	The CO2 laser showed less bleeding, delayed wound healing and pain removal, higher gingival recession, and no significant Clinical attachment loss findings compared to the diode laser
Kongsong, 2020[41]	Clinical study	50 patients	Trigeminal neuralgia	10600 nm	continuous mode	5 W	-	defocused	none	Patients' total daily doses of carbamazepine were significantly reduced. 94% of the patients had pain alleviation or no pain after CO2 laser neural ablation.
Kshirgar, 2020[42]	Case series	20 patients	Oral leukoplakia		Continuous mode	4-6 W	1 mm		None	After only one treatment, 90% of the patients who were being treated for a cure had local control. The second and third vaporizations were performed for the remaining 10%.
Dalirsani, 2021[43]	Case series	8 patients	Oral lichen planus	10600 nm	Continuous mode	4-7 W	0.2 mm	defocused	None	At follow-up visits, some patients developed mild keratotic lesions, and the majority of the patients were pleased with the treatment procedure.
Yao, 2020[44]	Case series	3 patients	Oral leukoplakia	-	-	-	-	-	None	The CO2 laser and PDT therapy together were secure and efficient with no negative side effects of note.
Taniguchi, 2022[45]	Animal study	72 rats	Socket preservation after tooth extraction	-	continuous wave	1 W	-	-	diode laser and control group	The two laser treatment groups had considerably less TGF-b1-positive regions and a-SMA-positive cells compared to the control group, and day 21 was similar for control and CO2 groups
Daigo, 2020[46]	Animal study	90 rats	Socket preservation after tooth extraction	10600 nm	Continuous wave	1 W	-	-	Diode laser	At an early stage of wound healing, new bone development and cancellous bone maturing were seen in the laser groups. Both treatment groups had considerably greater alveolar crest heights than the control group and had essentially no concavity in the mucosa of the extraction site. The quantity of myofibroblasts was also much decreased in the laser treatment groups compared to the control group.

Table 3. Continued.

First Author and year	Type of Study	Sample	The condition/lesion for using laser	Laser CO2 characteristics					comparison	Result of study
				wavelength	Emission mode	Average power	Spot diameter at the focus	Focus-to-tissue		
Kawamura, 2019[47]	Animal study	38 porcine keratinized gingiva sheet	Gingival tissue ablation	10600 nm	continuous wave	1 W	0.4 mm	-	Electroscalpel, Er:YAG, Er,Cr:YSGG, Diode, Nd:YAG lasers	With the CO2 laser, the surface temperature rose to its greatest during irradiation. As compared to other devices, Er,Cr:YSGG and Er:YAG produced less compositional surface change and smooth surfaces.
Foroughiasl, 2019[48]	Case report	2 patients	Mucocele	-	-	-	-	defocused	scalpel	After laser therapy, the healing process was quicker; there was no bleeding, and the patient's quality of life improved. In both final treatments, wounds healed adequately without recurrence after one year.
Matsumoto, 2021[49]	Case report	2 patients	Wharton's duct salivary stones	10600 nm	continuous wave	3 W	1 mm	-	none	The stones were successfully removed from both patients' sublingual glands without resulting in irregular bleeding, nerve damage, or other issues.
Chainani-Wu, 2022[50]	Case report	1 patient	Pemphigus vulgaris	10600 nm	continuous mode	3-5.5 W	-	-	None	After the surgery, the ulceration completely healed with no recurrence after two years.
Su, 2022[51]	Case report	1 patient	recurrent pyogenic granuloma	-	-	-	-	-	none	The pyogenic granuloma could be excised using a combined use of diode and CO2 lasers, fulfilling the patient's esthetic demands.
Hanna, 2019[52]	Case report	1 patient	Denture-induced hyperplasia	10600 nm	-	0.81 W	0.94 mm	-	None	Few to no postoperative problems were noted, and improved healing was shown after two weeks.
Soliman, 2019[53]	Case report	1 patient	Schwannoma of the tongue base	10600 nm	continuous super-pulsed mode	5-9 W	0.5 mm	focused	None	There was no substantial bleeding. The surgical procedure performed properly, the wounds healed adequately, and the swallowing abnormalities were corrected with no recurrence.
Roberts, 2022[54]	Case report	1 patient	Spongiotic gingivitis	9300 nm	-	0.4 W		-	none	Throughout the three treatment courses, no heat sensation or discomfort was noted by the patient. No treatment session showed tissue carbonization. Following the third treatment, there was no clinical recurrence, albeit there remained a persistent erythematous patch.

CO2: carbon dioxide, PVL: proliferative verrucous leukoplakia, OPMDs: Oral potentially malignant disorders, Er,Cr:YSGG: Erbium, chromium-doped yttrium, scandium, gallium and garnet, ND:YAG: Neodymium-doped yttrium aluminum garnet, Er:YAG: Erbium-doped yttrium-aluminum-garnet, PDT: Photodynamic therapy, NRS: numerical rating scale, TSS: Thongprasom sign score, .

and 21.6% at 50.6 months of the study.[20]

- Burning sensation: A study observed a burning sensation lasted 2–7 days and decreased over a month.[44] Others reported burning in 20%[22] and 37.5% of the patients.[43]
- The incidence of postoperative bleeding was 5.12%,[25] 5.8%,[19] and 6.6% of the subjects.[26]
- Other postoperative symptoms include superinfected lesions at a rate of 5.8%,[19] granulomas at a rate of 20%[21] and 7.7%,[18] edema and erosion,[44] erythema in all of the patients at the end of day 5,[22] and temporary numbness.[25] A research study also identified small bone necrosis at a rate of 8%, delayed wound healing at a rate of 4%, and sclerotic scars at a rate of 4%.[21]
- Lesion resolution rates were reported in 43.2%[20] and 47.4%[18] of the patients. The disease-free survival rate during the first year was 52.9% in a study.[18]

Oral Tumors

Nine research studies examined CO2 laser surgery for oral tumors. Oropharyngeal tumors were examined in a study. [27] Some studies found no complications.[53] The CO2 laser exhibited a higher recurrence rate between 4 and 15 months than the scalpel and Er,Cr:YSGG laser, despite non-significant differences.[28] In another study, the disease-free survival rate was 60% and the recurrence was 25%.[29] There was no evidence of recurrence in the 40-month or 10-year follow-up in a study.[53] Tenore et al. found the thermal effect of the CO2 laser was visible in all specimens and stronger in attached gingiva than in other anatomical locations.[30]

Another study found that when the excision of essentially normal marginal mucosa encircling the tumor is reduced, the recurrence of Oral Squamous Papillomas is markedly increased.[31] In a study, CO2 and Er,Cr:YSSG lasers improved the quality of scars after 4 weeks, had superior cosmetic results, and did not need a second treatment session compared to diode and Nd:YAG laser groups.[32] Gardenal et al reported 5% bleeding and 1% hematomas. No mucosal dehiscence, fistula, or wound infection occurred.[27]

Oral Fibrous-Epithelial Lesions

In a study, the nuclear and cytoplasm changes of the CO2, diode, Nd:YAG, and electric scalpel were higher than the Er:YAG and cold scalpel. The diode had the greatest loss of attachment, followed by the Nd:YAG, electric scalpel, CO2, Er:YAG, and cold scalpel. Also, carbonization was the highest in the CO2 and electric scalpel. The electric scalpel caused the most vascular changes, followed by the Nd:YAG, CO2, diode, Er:YAG, and cold scalpel.[33] Another study showed that there were considerable differences between the assessed thermal damage areas in the Er:YAG and CO2 lasers.[34] In addition, vestibuloplasty using the CO2 laser resulted in good healing, adequate vestibule depth, and healing after two weeks.[52]

Gingival Melanin Hyperpigmentation

Three studies evaluated gingival depigmentation by the CO2 laser. Nammour et al. found that the diode laser had the highest long-term stability, followed by CO2 and Er:YAG.[35] Moreover, Moeintaghavi et al found that the pulsed diode laser required less chair time than the CO2 laser.[37] In another study, the wound healed without scarring, infection, edema, or complications, improving its aesthetic look.[36]

Socket Preservation After Tooth Extraction

Two studies examined the impact of the CO2 laser on socket preservation following tooth extraction. The diode laser followed by the CO2 laser had the fewest a-SMA-positive cells and TGF-b1-positive areas following tooth extraction.[45] Another study found that on day 3 following extraction, CO2 had more osteoclast-like cells than diode and control groups, indicating active bone resorption. CO2 had fewer a-SMA-positive cells in the extraction socket and wound mucosa than the control group.[46]

Pyogenic Granuloma

Two trials evaluated the effectiveness of the CO2 laser in pyogenic granuloma surgery. In a study, after treatment, 55% of the patients exhibited transient erythema, 15% exhibited ulceration, 25% exhibited pigmentation, and one patient had blister. All of these symptoms gradually subsided.[38] In another study, following four months, the gingival wound completely healed with a healthy pink tint following CO2 combined with diode laser excision.[51]

Gingivectomy/Gingival Ablation

In a gingivectomy experiment, the CO2 laser tissue rupture was comparable to ER:YAG and higher than the scalpel. The coagulation layer width for the CO2 laser was greater than the scalpel, ER:YAG and ceramic bur.[39] In another study for gingival ablation, coral structures had many microcracks and holes after CO2 laser treatment. Er:YAG had the quickest operator-adjusted tip- movement, followed by CO2, scalpel, Er,Cr:YSGG, Diode, electro scalpel, and Nd:YAG.[47]

Other Conditions

In a study, the mucocele healed seven days following Co2 excision, with no complaints compared to scalpel excision.[48] In a study, Huge Wharton's duct salivary stones were removed by the CO2 laser in 10 minutes with no complications and abnormalities like ranula.[49] In a study by Kongsong et al for trigeminal neuralgia, surgical complications included transitory neurosensory impairment (82.0%) and temporary localized swelling (24.0%).[41] After the third ablation for spongiotic gingivitis, the subject reported no discomfort and

continued recovering, a smooth surface, and excellent esthetic results.[54] In frenulectomy surgery, in three of the five evaluated parameters, the diode laser performed better. [40] Chainani-Wu et al found no discomfort after 3 weeks. The interdental papilla and gingiva recovered with an excellent shape and a healthy, stippled surface that was rigid on the touch and exhibited no bleeding on probing.[50]

Risk of Bias

Table 4 displays the findings of each clinical trial and the information gathered for the risk of bias in each trial. We measured the risk of bias in 5 clinical trial studies.[24,34,35,37,40] The sequence generation was high in 3 articles.[24,35,37] The allocation concealment was high in one study.[35] Only in 2 studies, both the operator and the patient were blinded.[37,40] The other bias indicators were low in all studies. The overall risk of bias was low in only one study.[40]

Discussion

The strong affinity of the CO2 laser to water makes it a popular therapy for oral lesions such as fibromas, papillomas, and premalignant lesions.[9,57,58]

The CO2 laser alone or in combination with other therapies was beneficial in managing diseases that required minor oral surgery in most included studies. Some studies[18-21] discovered high recurrence rates following treatment with the CO2 laser. Multiple investigations have also indicated that this therapy has a high recurrence rate.[59-61]

Kuribayashi et al found a substantial association between surgical margins and oral leukoplakia recurrence. Patients having resection margins greater than 3 mm had a decreased recurrence rate, suggesting these margins to be the safest.[62]

A study found that at 6 months of therapy, individuals with at least a 3 mm margin had a decreased recurrence rate at 6 months compared to those with no margins.[63] These findings were also reported in some of our included studies.[18,19]

Deppe et al found that the continuous defocused mode had the lowest statistically significant recurrence rates, followed by the continuous mode with a scanner and the super-pulsed mode with a scanner. Other techniques with less thermal penetration could not access the cells that are deeper, resulting in greater recurrences.[64] In terms of methodology, compared to other techniques that included excision, the procedure in which total superficial ablation of the lesion was achieved in two sessions had a reduced success rate.[65]

Laser surgery, unlike cold-knife surgery, offers immediate sterilization and greater visibility, without physical tissue harm.[66] The following act as a concise summary of the benefits that come with using a CO2 laser: Ablation of tissues with precision, particularly; since the additional benefits of magnification and fine beam control of the operational microscope and microscope manipulator are considered; negligible damage to the neighboring tissues when the power density of the laser decreases significantly after passing this threshold as a consequence of energy absorbed by the tissue at which it is targeted; improved sight of the crucial bloodless operative area is made possible by the instant hemostasis effect of sealing tiny vessels; increased regular tissue recovering by reducing factors (like the quantity of myofibroblasts within the wound and the amount of the collagen matrix established) which cause scar tissue and wound contraction and also interfere with the function of oral soft tissue; construction of a physiological covering over the surgical site to reduce post-operative pain and tissue swelling; lastly, effective excision and destruction of all aberrant mucosa to minimize disease recurrence locally.[67,68] In addition, postoperative functional results, such as swallowing and speech, are improved as a result of the optimization of the broad excision achieved in comparison to cold tools and anatomically based resections.[69]

In a study on rats, the thermal effect of varied CO2 laser powers (3 W–12 W) was evaluated. The CO2 laser induced epithelial thermal damage comparable to dysplastic alterations, regardless of wattage. Hence, it was recommended that practitioners take these alterations into account.[70] Pulsed CO2 laser beams cause less thermal damage than the continuous wave in experiments.[71,72] A clinical investigation evaluated CO2 laser pulsed and continuous wave thermal injury results after excision biopsy of fibrous hyperplasia lesions. Both laser types caused equivalent thermal damage; hence, researchers suggested a 1 mm safety gap, particularly in the soft tissue lesions that are suspicious.[71] CO2 lasers and electrotomes were compared by Matsumoto. The electrotome caused

Table 4. Risk of Bias of the Included Clinical Trial Studies

Investigators	Sequence Generation	Allocation Concealment	Blinding of Study Participants and Personnel	All Patients Accounted for at the End of the Study	Clear Explanation of Withdrawals	Selective Reporting	Over Risk of Bias
Rosenthal, 2021[24]	High	Low	High	Low	Low	Low	High
Suter, 2019[34]	Low	Low	High	Low	Low	Low	High
Nammour, 2020[35]	High	High	High	Low	Low	Low	High
Moeintghavi, 2022[37]	High	Low	low	Low	Low	Low	High
Sfasciotti, 2020[40]	Low	Low	Low	Low	Low	Low	Low

more thermal damage than the CO2 laser, especially in pulsed mode.[73]

Hence, moving the handpiece frequently to minimize tissue heat buildup improves clinical safety with CO2 lasers. Moreover, to avoid unintentional exposure and interaction with the adjacent tissues, caution must be exercised. Considering the effect of temperature on bone tissues, prior studies showed that temperatures exceeding 47 °C caused osteonecrosis. Thus, adequate caution must be taken while irradiating tissues adjacent to bone using this laser.[47]

In terms of gingival depigmentation, because of its impact on the bone and tooth structures, a CO2 laser is unable to entirely remove melanin pigmentation from deep layers. In addition, the overstimulation, growth, and relocation of leftover pigment cells underlie the repigmentation following the CO2 laser therapy.[36] The ablation and penetration depth of a particular laser, which vary with wavelength and delivered energy density, could also have an impact on the outcomes. Hence, a certain wavelength with high absorption and shallow penetration would induce minimal heat production and superficial melanin layer breakdown. Variation in the gingival depigmentation procedure is an additional element that may account for the disparate results. The treatment will not succeed and the pigmentation will recur soon after if a certain procedure contributes to a partial removal of the functional melanocytes from the gingival epithelial.[35]

Some studies showed that soon after CO2 laser treatment, there is active bone remodeling inside the top surface of the extraction socket, preventing mucosal epithelial invasion.[46] The CO2 laser stimulated osteoblasts, osteoclasts, bone lining cells, undifferentiated mesenchymal stem cells, and bone marrow stem cells to differentiate and proliferate, initiating bone remodeling.[74,75]

Limitation and Suggestion

The usage of CO2 lasers has several restrictions, as discussed previously. These limitations include, in brief: uncertain recurrence rates in various conditions, especially in OPMDs; fewer esthetic outcomes compared to other treatments; increased epithelial thermal injury, which requires proper vigilance when irradiating tissues near to the bone with this laser.

Additionally, there are advantages of using the CO2 laser in surgery, including instant sterilization, improved vision, less post-operative discomfort and tissue swelling, efficient excision, and eradication of all abnormal mucosa.

In light of the laser settings used in the studies, we recommend utilizing a 10,600 nm wavelength and an average power of 1–10-win continuous mode, which produces excellent outcomes and fewer post-operative complications.

Conclusion

When considering the treatment options for oral mucosal disorders which require minor surgeries, CO2 lasers are one option that is worth considering, according to the analysis of the findings of all the research studies that were part of this study. In fact, there is yet no surgical procedure that can guarantee a patient will recover completely free of illness. Yet, as has been said, CO2 laser treatments of-ten result in shorter treatment duration, less adverse effects and problems during and after surgery, and less scarring. The practitioners should take into account both the biological and physical aspects of the CO2 laser in addition to those previously mentioned parameters; these parameters are favorable to positive patient psychology for both patients exploring treatment options as well as for outgoing patient types. CO2 laser treatment may be employed for managing various disorders. The findings of our study lead us to the conclusion that the CO2 laser in minor oral surgeries is effective, although more randomized clinical trials are re-quired to compare the results of CO2 laser surgery to those of other therapies and that multicenter studies might improve the conclusion.

Authors' Contribution

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Competing Interests

The authors declare no conflict of interest.

Ethical Approval

Not applicable.

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