Effect of diode laser fibrotomy in oral submucous fibrosis patients: Systematic review and Meta-analysis

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Abstract- Objective: To determine the effect of fibrotomy on mouth opening (MO) with diode lasers in patients with oral submucous fibrosis (OSMF).
Methods: Multiple databases were used to search for articles up to and including July 2022. Studies that reported using diode lasers for fibrotomy in OSMF patients were analyzed procedurally. Studies that fulfilled the inclusion criteria were then undertaken for qualitative and quantitative analysis.
Results: Five studies were included in this meta-analysis. The follow-up period ranged from 3 to 9 months. 980 nm was the wavelength of the diode lasers used in all the studies. Quantitative analysis showed a significant increase in MO after fibrotomy with lasers (Q value = 56.4, DF = 4, I2 = 92.91%).
Conclusion: Lasers benefit the patient and the surgeon more in fibrotomy procedures. More clinical trials evaluating additional clinical parameters would further validate the effects of laser therapy in OSMF patients. Lasers are safe, provide a clean surgical field, and heal with minimal scarring compared to the conventional use of a scalpel/blade.
Index Terms- Oral Submucous Fibrosis, oral fibrosis, diode lasers, trismus, lasers

I. INTRODUCTION

Oral submucous fibrosis (OSMF) is a chronic, progressive, scarring, high-risk precancerous condition of the oral mucosa seen primarily in the Indian subcontinent and South-East Asia. Pindborg and his associates defined Oral submucous fibrosis OSMF as "An insidious, chronic disease affecting any part of the oral cavity and sometimes the pharynx, occasionally preceded by vesicle formation, always associated with a juxta-epithelial inflammatory reaction followed by a fibro-elastic change of the lamina propria, with epithelial atrophy leading to stiffness of the oral mucosa, trismus and inability to eat" (1). OSMF is a progressive, and high-risk precancerous condition seen primarily in the Indian subcontinent and South-East Asia.
Various etiologic factors of OSMF reported in the literature include habitual areca nut usage, chilies, spicy foods, tobacco products, nutritional deficiencies, autoimmunity, and genetic susceptibility (2). The initial symptoms of OSMF include a burning sensation to spicy food and blanching of oral mucosa followed by the development of white fibrous bands leading to progressive difficulty opening the mouth (3). On microscopic examination, the epithelium shows atrophy and fibrosis (3).
OSMF may get resolved with cessation of the causative habits, mainly areca nuts, before forming fibrous bands in the oral cavity. Once fibrotic bands are formed inside the oral cavity, especially the buccal mucosa, it is complicated to manage the limited mouth opening (MO) and trismus along with other symptoms of OSMF. Various treatment modalities have been proposed and practiced, including dietary Vitamin A & B complex supplements, steroid or degradative enzyme injections, and surgical band excision with or without graft (4). Many studies have experimented with herbal agents such as Curcumin, Spirulina, Aloe vera, Tulsi, and tea pigments, but each has its limitation (5-7). Major hurdles in medicinal therapy are increased patient expense, longer duration of medicines, risk of adverse effects, and eventually non-compliance.
Lasers have multiple advantages in surgical procedures compared to scalpel/blade, including a cleaner operative field, less invasiveness, and minimal scarring and tissue damage post-operatively. Hence, due to the points mentioned above, diode lasers can be a valuable alternative option for surgical fibrotomy in OSMF patients (8).
These are the clinical situations wherein lasers might prove beneficial to scalpel (9). The diode laser, with its contact mode application and precision beam delivery, is gaining acceptance in multiple applications in soft tissue surgery, such as hemostasis, decreased scarring, and diminished post-operative pain are some of the advantages of laser to scalpel.
Systematic review/meta-analysis provides evidence on actual outcomes of the treatment from different studies; hence, the present study was performed to assess the effect of diode laser therapy on MO in OSMF patients.

II. MATERIALS AND METHODS

This study was registered at the "National Institute for Health Research PROSPERO, International Prospective Register of Systematic Reviews" (Registration number: CRD42022316736). Guidelines were taken from the "Preferred Reporting Items for Systematic Review and Meta-Analysis" (PRISMA) (10). The "PICO principle (i.e., "Patients," adults with OSMF; "Interventions," fibrotomy with diode laser; "Comparisons," none; "Outcomes," measurement of mouth opening (MO) in millimeters (mm))" was utilized for the development and addressing the following research question: "Does diode laser as

an adjunct to MO exercises, yields a favorable outcome in relieving limited MO/trismus in OSMF patients?"

Multiple databases, such as PubMed, Google Scholar, Science Direct, etc., were used for literature search, up to and including July 2022, for articles focusing on the research question. For the PubMed library, the following combinations of free textual words and MeSH (Medical Subject Headings) words were used: (Diode laser OR lasers) AND (oral submucous fibrosis OR oral fibrosis, OR chronic oral submucous fibrosis) AND (trismus/ mouth opening).

Three authors (ZA, HB, & AN) autonomously screened the articles for the selection and analysis of data. Any disagreement among the authors regarding study inclusion or exclusion was resolved through discussion and by referring a fourth reviewer (SR). Figure 1 describes the screening process according to the PRISMA guidelines. The following eligibility criteria were entailed for the inclusion of studies:

(1) Study design: Randomized control trials (RCTs) and clinical trials were included.

(2) Study participants: Diagnosed OSMF patients (aged ≥ 18 years), including both genders.

(3) Study groups: Patients who had fibrotomy with a diode laser.

(4) Outcome: MO (in mm).

In-vitro and animal studies, laser treatments other than diode laser therapy, a combination of laser therapies, case series and reports, and review articles were excluded.

Data extracted from the selected studies was the author's name, year of publishing, participant's age, gender, follow-up period, features of laser equipment, and study outcomes. All reviewers crosschecked the data obtained from selected studies, and all discrepancies were resolved after discussion.

Meta-analysis was done to assess the outcome of the selected studies. The I2 and Q-statistics were used to assess the heterogeneity among the studies included in this analysis. Forest plots were used to report the outcome's weighted mean difference (WMD) and 95% confidence intervals (CI). The pooled effect is considered statistically significant if the p-value is < 0.05. For determining the level of heterogeneity supposition, Cochrane Q was determined. The I2 statistic was applied to quantify inter-study variability having a range of 0 to 100%, with 0% indicating no heterogeneity, whereas the increased values indicate a higher level of heterogeneity. Statistical software (MedCalc) was used for the analyses.

III. RESULTS

Study selection

Thirty-five study titles and abstracts were initially identified in the following databases: PubMed, EMBASE, Science Direct, Google scholar, and SCOPUS. Duplicate studies and those irrelevant to the focus question were excluded. Fourteen research papers were excluded from the total nineteen papers selected for full-text reading. Five studies were finally selected and processed for data extraction. Figure I show the flow chart of study selection according to PRISMA.

Characteristics of included studies

All the studies were conducted in India and included patients with chronic OSMF (11-15). All used the combined approach of MO exercises with diode laser fibrotomy. Three studies had a follow-up period of 6 months (11-13), while Gupta et al., 2018 had a follow-up period of 9 months (14), and another one had only three months (15).

Quality of the clinical studies

The studies included in this analysis were clinical trials and RCTs. The sample size was sufficient in three (11, 12, 14) of the studies (n = 30 - 50) whereas two (13, 15) studies had a smaller sample size of (n = 10 - 12). A pre-submitted checklist based on the recommended revisions of the Consolidated Standards of Reporting Trials was used to conduct the present analysis (16). The risk of bias was estimated for each selected study based on the "Cochrane Handbook for Systematic Reviews of Interventions: (1) low risk of bias (when all criteria were met); (2) high risk of bias (when ≥ 1 criterion was not met); and (3) unclear (when ≥ 1 criterion was partially met)" (Table III).

Test for heterogeneity

The Q test and I2 test were calculated to identify the level of heterogeneity, as the values of the level of inconsistency were within 95% of CI. A random-effects model was used to assess the pool effects (Table I).

Synthesized Findings

The overall findings of this analysis showed a significant increase in MO of patients with OSMF after laser fibrotomy. The pool effects in terms of standardized mean difference as obtained in a fixed effect model showed an impact of 1.9 in laser fibrotomy that, according to the Cohen rule of thumb, depicts a significant effect (Table I). I2 value was 92.91 % which shows a high level of heterogeneity among the studies (Table I).

IV. DISCUSSION

Among the clinical aspects of OSMF, limited MO due to the formation of fibrotic bands remains the biggest challenge for clinicians and the patient itself. This limitation results in poor oral hygiene; if the tobacco habit continues, it may eventually lead to oral cancer. Therefore, the focus should be on improving the patient's ability to open their mouth normally. This would enhance the ability to chew, swallow, maintain oral hygiene and speech, and thus further helps in achieving better oral health-related QoL (OHRQoL) in those patients (17).

Due to the progressive and insidious nature of the disease, in OSMF patients, trismus does not revert spontaneously or even after cessation of betel nut chewing. Many treatment modalities have been developed over the past years but have been mostly ineffective in improving the disease condition.

Oral or topical medicines have proven insufficient in reducing trismus or other OSMF-related symptoms. Surgical management of OSMF includes the excision of fibrotic bands (fibrotomy) in the oral cavity either by a scalpel/blade or soft tissue lasers. Fibrotomy is usually but not always, followed by a tissue graft taken from the host's body itself to maintain the oral opening (18).

The site and type of incision can influence the resultant increase in MO. 'Inverted Y shape' incision in the retromolar region and buccal mucosa was observed to reduce trismus significantly in a few studies (19, 20). Another study reported a significant increase in MO with the help of 'multiple parallel'

incisions (21). However, a study reported that they had excised fibrous bands in the soft palate and anterior faucial pillars in addition to the retromolar region and buccal mucosa under general anesthesia (GA), which could assist the former findings of this study (21). Few studies worked on 'linear' incisions and reported relatively lower outcomes than other studies (13, 14, 22).

Post-surgical fibrosis and donor-site morbidity are the potential complications of conventional fibrotomy with a scalpel/blade. Local physiotherapy, including hot rinses and short-wave diathermy, did not evoke satisfactory results.

Lasers are becoming a significant part of therapy in dentistry. The sight of a scalpel and blade results in patient anxiety and causes difficulty in managing the operative field. On the other hand, Lasers provide a clean working environment and leave minimal scarring, becoming a priority for patients.

The rationale for using laser for surgical fibrotomy in OSMF is photothermal action, resulting in tissue disruption by sufficient heat deposition to vaporize the tissue (23). Energy immitted by lasers is absorbed selectively in the target tissues and results in a direct tissue cut (cold cut) or causes tissue rupture due to the vaporization of water within a cell (thermo-mechanical tissue ablation). This mechanism limits the collagen damage up to 5 μm (approximately two cell widths), sparing the extracellular collagen matrix.

In general, laser-related parameters such as laser type, wavelength, energy used, and exposure time play an essential role in securing desired effects of laser therapy (24). In addition, the target tissue's optical properties and absorptive nature determine the laser energy needed to achieve successful outcomes. However, due to the unavailability of a scientific basis for the selection of laser type to date, the choice is dependent mainly upon the availability of the equipment in the set-up and the personal experience of the dental surgeon.

We found a few other studies similar to the ones included but were not part of the meta-analysis. A study reported a significant difference in MO after fibrotomy with laser but was not used for the analysis as they did not mention the standard deviation (SD) in their results (22).

Though diode lasers are the first choice for oral fibrotomy, Erbium Chromium Yttrium Scandium Gallium Garnet (ErCr: YSGG) lasers are also used for the said purpose (20). Similarly, Potassium titanyl phosphate (KTP) lasers have also been utilized in fibrotomy procedures (21, 25), but not many studies have reported its use. In the future, a comparative analysis of the different laser techniques would be beneficial to determine which type is more efficient.

The study's limitations were its small sample size for quantitative analysis. Secondly, there was no comparison between the efficacy of surgical incisions with scalpel/blade and lasers. Further studies with proper laser protocols are warranted to determine which method of fibrotomy would lead to better results in terms of MO, keeping in mind the types and sizes of incisions being made.

V. CONCLUSION

Lasers are a promising advancement in dentistry, being used in basic procedures such as teeth whitening and caries removal to more advanced surgical procedures such as wound healing, removal of soft and hard tissues, photodynamic therapy for malignancies, etc. More studies with uniform guidelines and protocols are required to strengthen its use for practitioners.

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Table I: Pooled effects of Fibrotomy with diode laser on the increase in MO in SMD.

Study	N1	N2	Total	SMD	SE	95% CI	t	P	Weight (%)	
									Fixed	Random
Lokesh *et al*, 2014	50	50	100	2.2	0.3	1.7 to 2.7			39.76	24.31
Agarwal *et al*, 2015	30	30	60	0.9	0.2	0.4 to 1.4			34.85	24.20
Mudigonda *et al*, 2016	12	12	24	3.5	0.6	2.1 to 4.8			6.17	20.74
Gupta *et al*, 2018	30	30	60	2.9	0.4	2.1 to 3.6			18.68	23.47
Vatsa *et al*, 2018	10	10	20	13.4	2.2	8.9 to 17.9			0.53	7.27
Total (fixed effects)	132	132	264	1.9	0.16	1.7 to 2.3	12.6	<0.001	100.00	100.00
Total (random effects)	132	132	264	3.1	0.69	1.7 to 4.5	4.5	<0.001	100.00	100.00
Test for heterogeneity: Q value = 56.4, DF = 4, P value < 0.0001, I^2 = 92.91%										

Table II: Parameters of the included studies.

Studies	Sample size	Gender, age	Laser details	Adjunct treatment	Duration of treatment
Lokesh *et al*, 2014	100	Both genders, 18-50 years	980 nm, diode laser (fiber width 600 µm diameter, 6 W)	MO exercises, multi-vitamin & antioxidants	6 months
Agarwal *et al*, 2015	60	Both genders, 18-57 years	Diode laser (10 W)	MO exercises	6 months
Mudigonda *et al*, 2016	24	Both genders, 24-46 years	Diode laser (5 W)	MO exercises	6 months
Gupta *et al*, 2018	30	Both genders, 20-50 years	980-nm, diode laser	MO exercises & topical corticosteroid	9 months
Vatsa *et al*, 2018	10	Both genders, 32.4±12.6 years	Diode laser, spot size of 0.2 mm continuous mode (10 W)	Prophylactic antibiotics	3 months

Table III: Evaluation of bias risk in the included studies.

Studies	**Random sequence generation**	**Allocation concealment**	**Blinding of participants & personnel**	**Blinding of outcome assessment**	**Incomplete outcome data**	**Selective reporting**
Lokesh *et al*, 2014	1	1	3	1	1	1
Agarwal *et al*, 2015	1	3	2	1	1	1
Mudigonda *et al*, 2016	1	2	1	1	1	1
Gupta *et al*, 2018	3	3	3	1	1	1
Vatsa *et al*, 2018	2	2	2	2	1	1

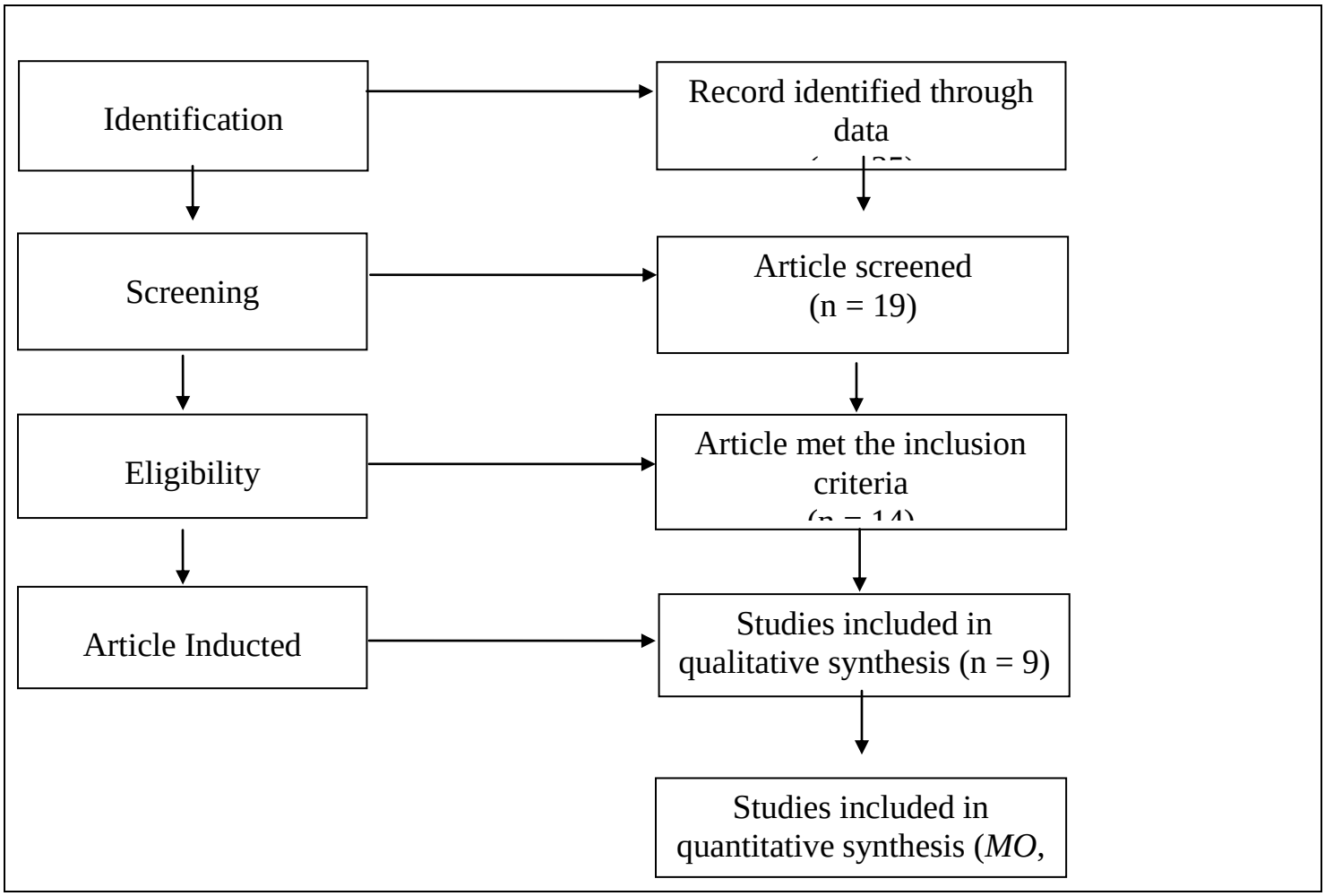

Figure I: Flow diagram according to PRISMA guidelines.

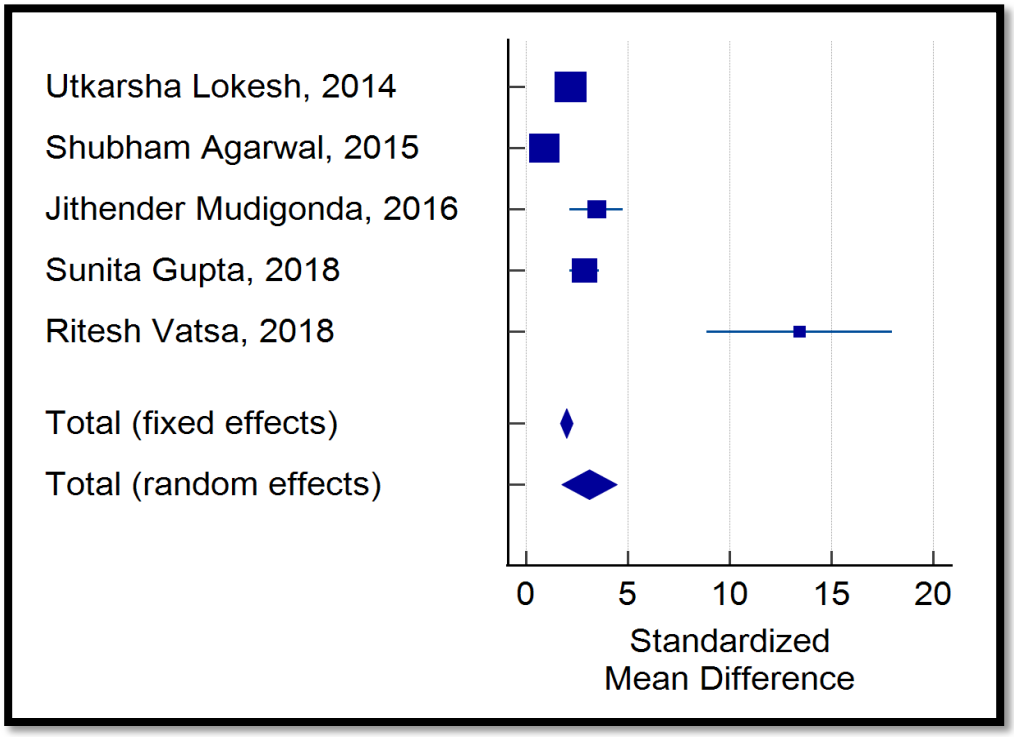

Figure II: Forrest plot of the studies included in the meta-analysis.