Treatment outcomes of laser therapy in oral submucous fibrosis-a systematic review

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ABSTRACT

Background: The mainstay of oral submucous fibrosis (OSF) management is to increase the mouth opening; thereby improving oral functionalities. In modernized dentistry, laser therapy (LT) could play a major role for trismus relief in OSF patients. The present review was performed to systematically analyze the published literature on LT for OSF management.

Methods: PubMed, Scopus, Web of Science and CINAHL databases were searched until June 2019 using suitable key words and the information was extracted according to the PRISMA guidelines. All full text papers that assessed efficacy of LT for OSF management without limitations on age, gender, ethnicity, or socioeconomic status of the participants were considered eligible. Participants were allocated to the LT alone or in adjunct to oral physiotherapy and medicinal treatment. Outcome parameters included the reduction in trismus. Review articles, case reports, editorial, conference abstracts and in vitro studies were excluded. No restriction was applied on date and language of the publications.

Results: Out of 97 published papers, 7 studies met the inclusion criteria and were included for the analysis. All the studies were clinical and mainly included stage II and III OSF patients. Although different laser types and other parameters were used, all the studies reported improvement in mouth opening in the range of 6.84 mm and 23.7 mm. Additionally, two studies noticed reduced burning sensation and increased tongue protrusion and cheek flexibility. **Conclusion:** The LT can provide a promising and better means for relieving trismus and probably OSF-related other symptoms in moderate stages of the disease.

1. Introduction

Oral submucous fibrosis (OSF) is a high-risk premalignant condition of the oral mucosa involving the oropharynx. It is characterized by excessive fibrotic changes in the lamina propria and the associated connective tissue of oral mucosa.¹ The rate of malignant transformation of OSF is about 7–30%.² Although highly predominant in Indian sub-continent and other Asians,³ OSF is gradually spreading all over the world including Europe and America due to Southern Asian immigrants

population.^{4,5} OSF results in blanching and stiffness of the oral mucosa, trismus, burning sensation in the mouth and hypomobility of the tongue with loss of taste sensation, leading to compromised quality of life (QoL).^{6,7}

OSF may be resolved with cessation of areca nut/betel quid chewing habits if it is noticed before initiation of trismus.⁸ Once initiated; it is difficult to control the progression of trismus. In initial stages of OSF, various medical treatments have been used over the past decades with limited benefits.⁹ As OSF is a chronic disease, longer use of medications

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increases patient's expenses, non-compliance and risk of adverse systemic effects.¹⁰ Surgical approaches advocated for advanced stage of the disease has associated intra-operative bleeding, post-operative pain and relapse due to fibrosis of the surgical wound and many times ends up in disappointments for the clinicians and patients. Even though electro-surgical approaches ensue reduced bleeding, it induces deep tissue damage followed by increased post-operative fibrosis.^{11–15} At present, there is no consensus on management of group II and III OSF as conservative treatment does not provide much benefit and aggressive surgical techniques are not justified in these cases.

Traditionally, treatment outcomes in OSF patients have been assessed by reduction in trismus. Increasing the mouth opening (MO); being considered as the mainstay of treatment in OSF, the advent of lasers (light amplification by stimulated emission of radiation) in recent years has been continuously attracting the attention of researchers and clinicians due to its effectiveness in relieving OSF symptoms. With multiple advantages over current techniques including bloodless operative field, minimal invasiveness, reduced fibrosis, scarring and tissue shrinkage after complete healing, lasers can be employed as a valuable alternative option for surgical fibrotomy in OSF patients.

Increasing the MO in OSF patients has always been a hot topic in the scientific community with past decades witnessing a bloom of studies focused on surgical fibrotomy to reduce OSF-related trismus and other symptoms. However, there was still lack of firm clinical evidence to support the effectiveness of laser therapy (LT). Systematic review/meta-analysis provides evidence on actual outcomes of clinical efficacy and safety. With this background, the present systematic review was performed aiming to synthesize the available evidence from the series of studies to assess the laser treatment outcomes in OSF patients.

2. Materials and methods

This systematic review was carried out following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement¹⁶ (Supplementary material 1) and was not published or registered in advance. Taking into consideration the nature of the current study no approval by an institutional review board was necessary.

2.1. Focused PICO question

PICO question¹⁷ was defined for screening the qualified studies: “does LT have an effect in management of OSF?” 1-Population: patients with OSF, 2-Intervention: LT, 3-Comparison: medicinal treatment/oral physiotherapy as an adjunct, or alone to LT, 4-Outcome: Benefits or lack thereof: reduction of trismus, burning sensation and other OSF-related symptoms.

2.2. Literature search

The PubMed, Scopus, CINAHL and Web of Science were searched for all the publications describing LT in OSF without language limitations on 20th June 2019. As per the search strategy (Supplementary material 2 & 3), all the relevant papers were identified. In addition, the reference lists of all relevant articles were also hand-searched to ensure a thorough screening process.

2.3. Eligibility criteria

Studies enrolled in the systematic review must meet the following inclusion criteria: (a) studies that evaluated efficacy of LT for management of OSF; (b) all the participants were definitely diagnosed as OSF through clinical manifestations; (c) participants went through LT without limitations on age, gender, ethnicity, or socioeconomic status; (d) participants were allocated to the LT alone or in adjunct to oral physiotherapy and/or medicinal treatment; (e) the follow-up time was at least 3 months after laser therapy; (f) primary outcome variables

included reduction in trismus and secondary variables, if available included burning sensation and other OSF-related symptoms and (g) studies without restriction on date and language of the publications.

The exclusion criteria encompassed: (a) studies characterized as review articles, case reports, editorial, conference abstracts, correspondence and in vitro studies; (b) patients with any systemic disease or on any medication that could interfere with the mouth opening range; (c) studies with missing data; (d) studies on photodynamic therapy and (e) if full paper not available.

2.4. Study selection

Two reviewers (SG and AG) independently screened titles and abstracts of the relevant articles for their eligibility. Full texts of all potentially eligible papers were then retrieved and further evaluated to identify studies that met all inclusion criteria. Any discrepancies were resolved by discussion with third reviewer (SS) and a list of the articles to be included in this review was finalized.

2.5. Data extraction

Two reviewers (SG and AG) independently assessed all the included studies to extract the information such as number of patients, gender, age, stage of OSF, LT details, type of anesthesia, site of incision, type of incision, adjunctive treatment, results, follow up and quality of life analysis. Any disagreements were resolved by discussion with third reviewer (SS).

3. Results

3.1. Search results

The initial search yielded a total of 97 hits (PubMed: 22, Scopus: 36, CINAHL: 12, and Web of Science: 27). After removal of duplicates ($n = 46$) and screening of titles and abstracts, 9 full texts were agreed for further evaluation, of which 7 met the inclusion criteria. Fig. 1 demonstrates an overview of the search process.

3.2. General characteristics of included studies

The characteristics of all included studies are summarized in Table 1. All the studies^{11–15,18,19} were clinical and published between 2005 and 2008. In terms of study design, all the studies were observational cross-sectional in nature and there was not a single study on randomized controlled trial. Most commonly used classification system used for grading OSF was of Khanna and Andrade.²⁰ All the studies^{11,12,14,18,19} included stage II and III OSF patients except for one which included stage III and stage IVA patients.¹³ The number of study participants ranged between 8 and 30 and the mean age was between 27 and 35.8 years. Only one study did not report gender distribution of the subjects,¹¹ while remaining six studies had majority of the male subjects.^{12–15,18,19} The follow-up period across studies ranged from 3 to 36 months.

3.3. Laser-related characteristics of included studies

Three different types of lasers were used in the included studies. Amongst these, diode laser was used in majority of the studies ($n = 4$)^{11,13,18,19} whereas KTP-32 and ErCr:YSGG lasers were employed in two^{12,14} and one study¹⁵ respectively. Nayak et al.,¹⁴ Choudhary et al.,¹⁵ Mudigonda et al.¹⁸ and Gupta et al.¹⁹ reported power density of the laser used which were 8 W/cm², 1.5 W/cm², 5 W/cm² and 2 W/cm² respectively. The wavelength (980 nm) of the laser used was reported by Gupta et al.¹⁹ only and none of the included studies reported the treatment time of the laser application. Amongst 7, four studies have performed laser fibrotomy under general anesthesia (GA).^{11–14}

Fig. 1. PRISMA flowchart describing the identification, selection and inclusion of studies.

However, remaining three studies have used local anesthesia (LA).^{15,18,19}

Three amongst 7 studies used 'linear' incision for laser fibrotomy.^{13,18,19} 'Inverted Y shape' incision was employed by two studies^{11,15} whereas Kameshwaran et al.¹² and Nayak et al.¹⁴ worked by 'Z' shape and 'multiple parallel' incisions respectively. Majority of the studies reported retromolar region and buccal mucosa as the selected sites for surgical fibrotomy. However, in addition to these sites, Nayak et al.¹⁴ also excised fibrous bands in the anterior faucial pillars and soft palate.

All of the seven studies have advised oral physiotherapy in adjunct to LT^{11–15,18,19} and five studies have further supplemented medications including antioxidants, topical/intralesional steroids.^{12–15,19}

3.4. Outcomes of studies

All the studies reported improvement in the MO abilities of the participants with somewhat varied results. The average increase in the MO ranged between 6.84 mm and 23.7 mm. Amongst 7, six studies^{11,12,14,15,18,19} showed significant improvement in MO after LT and Talsania et al. reported highly significant results.¹³ Mudigonda et al.¹⁸ and Gupta et al.¹⁹ also reported significant reduction in the burning sensation. Furthermore, tongue protrusion and cheek flexibility was noticed to be significantly increased after LT in one study.¹⁹ Mudigonda et al.¹⁸ compared the effects of diode laser and medications (steroid & hyaluronidase injections) in their study and found greater significance in average increase in MO and decreased burning sensation in patients treated with diode laser. In addition, Choudhary et al.¹⁵ reported improvement in oral health-related QoL (OHRQoL) as recorded by OHIP-14 scores.

3.5. Adverse effects

None of the included studies reported any side effects of using LT.

4. Discussion

Among various debilitating aspects of OSF,^{21,22} trismus due to fibrosis remains the main challenge for the clinicians and researchers. The OSF-related trismus hampers self-cleansing activity of the stiff oral tissues; thereby increasing the contact of betel nut and tobacco carcinogens with the tissues and thus increases the probability of malignant transformation. Recently, Gadabail et al.²³ also suggested stiff and rigid oral tissues in OSF patients as initiator and promoter of carcinogenesis. Therefore, the treatment of OSF patients should primarily be directed towards improving the MO and increasing flexibility of the oral mucosa. This definitely augments the chewing ability, swallowing, oral hygiene care, speech, nutritional status; and thus further helps in achieving better OHRQoL in this population.

Because of the chronic, progressive and insidious nature, OSF-related trismus does not regress either spontaneously or with the cessation of betel quid chewing. The management of OSF over the past decades has been varied and largely ineffective. Medical management with various options is inadequate in reducing trismus and other OSF-related symptoms.⁹ The potential complications of post-surgical fibrosis leading to recurrence and donor-site morbidity downcast the outcomes of surgical approaches.²⁴ Local physiotherapy including hot rinses, short wave diathermy did not evoke satisfactory results.²⁵ However, LT provides clinicians and researchers a new minimally invasive, cost- and time-effective treatment option for OSF patients. As it produces immediate trismus relief with uneventful healing, LT enhances patients

Table 1
General characteristics of the studies included.

Sr. no.	Author (Year)	No. of patients	M/F	Mean age (Yrs)	OSF stage	Laser used			Type of anesthesia	Site of incision	Type of incision	Adjunctive treatment	Results (average increase in mouth opening in mm)	Follow up (months)	QoL
						Source	Wave length (nm)	Power density W/cm ²							
1	Shah et al. ¹¹ (2005)	10	NA	27	II,III	Diode	NA	NA	General	RM, BM	Inverted “Y” shape	OP	Group II- 15	3	NA
2	Kameshwaran et al. ¹² (2006)	15	15/0	29	II,III	KTP 532	NA	NA	General	PMR, FP	“Z” shape	OP, antioxidants, intralesional steroids	Group III- 17 12.6	12	NA
3	Talsania et al. ¹³ (2009)	8	8/0	27	III, IVA	Diode	NA	NA	General	Anterior FP, RM trigone, BM	Linear	OP, antioxidants	15	18–36	NA
4	Nayak et al. ¹⁴ (2009)	9	9/0	35.8	III	KTP 532	NA	8	General	Anterior FP, RM trigone, SP, BM	Multiple parallel	OP, antioxidants	23.7	12	NA
5	Choudhary et al. ¹⁵ (2013)	16	10/6	32.3	II,III	ErCr: YSGG	NA	1.5	Local	RM region, BM	Inverted “Y” shape	OP, antioxidants, topical steroids	17.5	12	Improved OHRQoL
6	Mudigonda et al. ¹⁸ (2016)	Laser gp- 12 Medication gp- 12	22/2	31	II	Diode	NA	5	Local	RM region, BM	Linear	laser group- OP, medication group- Steroids and hyaluronidase injections	Laser gp- 6.84 Medication gp- 1.34, In addition, decreased burning sensation (greater in laser gp)	6	NA
7	Gupta et al. ¹⁹ (2018)	30	22/8	29.7	II,III	Diode	980	2	Local	BM	Linear	OP, topical steroids	7.7 In addition, Decreased burning sensation, increased tongue protrusion & cheek flexibility	9	NA

Note- OSF: Oral submucous fibrosis, NA: Not available, RM: Retromolar, BM: Buccal mucosa, PMR: Pterygomandibular raphe, FP: Faucial pillars, SP: Soft palate, OP: Oral physiotherapy, OHRQoL: Oral health-related quality of life.

satisfaction and help motivate them for continuation of further treatment.^{26,27} More importantly, being delivered through a flexible cable, lasers can be targeted to relatively difficult-to-access areas with ease and safety. Despite of all these advantages, the literature on role of lasers in OSF treatment is still lacking. Therefore, there was a dire need of evaluating the influence of LT for management of OSF patients.

Rationale for the use of LT for surgical fibrotomy in OSF is photo-thermal action which results in disruption of the tissue by sufficient deposition of heat to vaporize the tissue.²⁸ Interestingly, the laser energy is absorbed selectively in the target tissues and results in a direct tissue cut (cold cut) or cause tissue rupture due to vaporization of water within a cell (thermo-mechanical tissue ablation). This mechanism limits the collagen damage up to 5 µm (approximately 2 cell widths) sparing the extracellular collagen matrix.

In general, the laser-related parameters such laser type, wavelength, energy used and exposure time play an important role to secure desired effects of the LT.²⁹ In addition, target tissue's optical properties, and its absorptive nature determines the laser energy needed in achieving successful outcomes of LT. However, due to unavailability of scientific basis for selection of laser type till date, choice is mostly dependent upon the availability of the equipment in the set-up and the personal experience of the dental surgeon. Majority (57%) of the studies^{11,13,18,19} included in this review used diode lasers. The diode laser is a semiconductor laser and has a wavelength in the range of 800–980 nm. It emits through fibre-optic cable and has a reasonable cutting efficacy without damaging dental hard tissues. Although, limited literature is available on role of diode lasers in OSF, it has shown successful outcomes in gingivectomies, frenectomies, gingival depigmentation, scaling and root planning etc.^{30–32} The KTP-532 laser works on wavelength of 532 nm that is selectively absorbed by blood vessels; thus providing excellent haemostatic characteristics. Kameshwaran et al.¹² and Nayak et al.¹⁴ reported significant role of KTP-532 laser in increasing the MO in OSF patients. An ErCr:YSGG laser has 2780 µm wavelength. This wavelength is well absorbed by water and can be used on oral soft tissue without causing thermal damage.³³ Significant results has been noticed by Choudhary et al. for trismus relief in OSF patients using ErCr:YSGG laser.¹⁵

Four of the seven studies used GA and belonged to decade 2000s.^{11–14} However, other three studies performed surgical fibrotomy under LA.^{15,18,19} All these studies were in the current decade of 2010s, suggesting a changing protocol for use of lasers in the management of OSF. It is important to note that use of GA always have an added risk of managing airway apart from other associated endangers. In addition, procedure performed under GA is time-consuming and adds extra cost to the patient. In contrast, laser fibrotomy can be performed on a dental chair or a minor operating room under LA; thus, is less time consuming. Moreover, the procedure is without any associated risk of GA and cost-effective as it cuts extra financial burden of hospital administration and post-operative care on patients. Thus, it is quite conceivable that laser fibrotomy under LA can serve as an effective and affordable treatment option for OSF patients in Asian countries where majority of the patients belong to lower socio-economic strata.³⁴

The site and type of incision of the laser fibrotomy can influence the resultant increase in MO. Choudhary et al.¹⁵ and Shah et al.¹¹ observed significant results in reducing trismus by using 'Inverted Y shape' incision in retromolar region and buccal mucosa. Nayak et al.¹⁴ accomplished excellent outcomes with the help of 'multiple parallel' incisions. However, this is supported by the fact that they have excised fibrous bands in the soft palate and anterior faucial pillars in addition to retromolar region and buccal mucosa under GA.¹⁴ Three studies worked on 'linear' incision and reported relatively less effective outcomes as compared to those of other included studies.^{13,18,19}

Apart from relieving trismus, it is essential to therapeutically target other OSF-related symptoms to achieve successful outcome goals in OSF management and improve the OHRQoL of patients. The burning sensation was found to be significantly decreased in two studies^{18,19} in

addition to increased cheek flexibility and tongue protrusion as reported by Gupta et al.¹⁹ It is important to note that rigorous daily oral physiotherapy should always be used adjuvant to laser fibrotomy in order to sustain the resultant increased MO.^{11–14} We believe that patient counseling and motivation plays a crucial role to increase their compliance and in regard to habit cessation. All the studies included in this review implemented oral physiotherapy after laser fibrotomy and achieved good outcomes for longer time. Medicaments including antioxidants, corticosteroids and hyaluronidase are vitally important supplements and plays pivotal role in the success of OSF treatment. Six studies included in the present review have advised antioxidants/steroids in addition to LT.^{12–15,18,19} Due to non-inclusion of appropriate control groups in the included studies, the degree of MO attributed to these adjunct therapies (physiotherapy and medicine) cannot be expressed. Moreover, appropriate randomization of the samples is warranted in the future research.

5. Limitations and strengths

One of the major limitations of this study is the heterogeneity of the laser type and other parameters used in the included studies. In addition, there was diversity in sample size, age, gender and duration of follow-up. Present systematic review has only one study on comparison of LT with other therapeutic approaches.¹⁸ Hence, meta-analysis of the studies was not carried out. Despite of these limitations, the present study is the first systematic appraisal to review the efficacy of LT for OSF management and it has provided the most recent and relevant evidence that can be helpful for the clinicians and researchers.

6. Conclusions

The present systematic review identified three different lasers that were used for management of OSF. The noteworthy finding of this systematic review was lasers can provide a promising and better means for relieving trismus and probably OSF-related other symptoms in moderate stages of the disease as they are minimally invasive, well tolerated, time- and cost-effective with sustainable outcomes and lesser morbidity. The observations of this review can help enhance awareness among the healthcare professionals and clinicians about various lasers and probably will also be a part of their practice. We recommend future research with appropriate study designs to implement laser therapy for increasing mouth opening and to assess the therapeutic efficacy of lasers in minimizing the other signs and symptoms of OSF.

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Declaration of competing interest

None declared.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.jobcr.2020.05.004>.

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