https://doi.org/10.48047/AFJBS.6.12.2024.5663-5672

African Journal of Biological Sciences

Journal homepage: http://www.afjbs.com

Research Paper Open Access

Comparative evaluation of Low-Level Laser Therapy with Intralesional Injections and Intralesional Injections alone for the treatment of Grade-II OSMF

Dr.Preeti Upadhyay[1], Dr.Manish Bhalla[2],Dr.AnshikaSharma[3],Dr.Anupama Pradhan[4] , Dr. Arpita Goswami[5], Dr. Saurabh Kumar[6]

1. Dr. Preeti Upadhyay- Professor and Head of Department, Department of Periodontology, Inderprastha Dental College and Hospital, Sahibabad, Ghaziabad,India.
2. Dr. Manish Bhalla, Professor, Inderprastha Dental College and Hospital, Sahibabad, Ghaziabad,India.
3. Dr. Anshika Sharma-Post Graduate Student, Department of Periodontology,Inderprastha Dental College and Hospital, Sahibabad, Ghaziabad, India.
4. Dr. Anupama Pradhan-Post Graduate Student, Department of Periodontology, Inderprastha Dental College and Hospital, Sahibabad, Ghaziabad, India.
5. Dr. Arpita Goswami- Reader, Department of Periodontology, Inderprastha Dental College and Hospital, Sahibabad, Ghaziabad, India.
6. Dr. Saurabh Kumar- Senior Lecturer, Department of Periodontology, Inderprastha Dental College and Hospital, Sahibabad, Ghaziabad, India.

Correspondingauthor-**Dr.AnshikaSharma,**

Email- anshikasharma251@gmail.com, Address-Inderprastha Dental College and Hospital, Sahibabad,Ghaziabad,India.

Article History
Volume 6, Issue 12, 2024
Received: 30 June 2024
Accepted: 20 July 2024
Doi:
10.48047/AFJBS.6.12.2024.5663-5672

ABSTRACT:

INTRODUCTION: OSMF stiffens oralmucosa, reducing mouth opening and causing burning sensation, affecting oral health and overall quality of life. Therapies such as intralesional injections stimulate tissue growth. The use of lasers is known to alleviate OSMF symptoms.The objective of this study was to evaluate and compare the efficacy of Low-level laser therapy with intralesional injections and intralesional injection alone for the treatment of OSMF.

METHODOLOGY: 20 individuals with OSMF were randomly split into two groups of ten each to evaluate, changes in mouth opening, and pain response to treatment. One groupreceived solely Intralesional Injections, while second group received both Intralesional Injections and Low-level laser therapy.

RESULT: Regarding mouth opening, the Intralesional Injection + LLLT group exhibited notably superior progress, compared to the Intralesional Injection alone group. However, no significant contrast was observed between the groups in terms of pain sensation.

CONCLUSION: The findings of this study affirm that combining LLLT with intralesional injections is a viable treatment approach for patients with OSMF.

INTRODUCTION: Oral Submucous Fibrosis (OSMF) represents a significant premalignant condition affecting the oral mucosa, particularly in the oropharynx region. It manifests through pronounced fibrotic changes within the lamina propria and associated connective tissues of the oral mucosa.[1] The malignant transformation rate of OSMF ranges from 7% to 30%.[2] Although prevalent among populations in the Indian subcontinent and other Asian regions[3], OSMF manifests with characteristic symptoms such as blanching and rigidity of the oral mucosa, trismus, oral burning sensation, tongue hypomobility, and taste sensation loss, all contributingto compromised Quality of Life (QoL)[4]. Cessation of areca nut/betel quid chewing habits may resolve OSMF if identified before the onset of trismus.[5] However, once trismus initiates, controlling disease progression becomes challenging.[6] Over past decades, various medical treatments have been employed with limited efficacy due to the chronic nature of OSMF, leading to increased patient expenses, non-compliance, and risk of adverse systemic effects.[7] Surgical interventions for advanced OSMF stages entail intraoperative bleeding, post-operative pain, and relapse due to surgical wound fibrosis, often resulting in dissatisfaction for both cliniciansandpatients.Althoughelectro-surgicalapproachesofferreducedbleeding,theyinduce deep tissue damage and subsequent post-operative fibrosis.[8] Traditional evaluation of treatment outcomes in OSMF patients has focused on trismus reduction, with increasing mouth opening (MO) consideredpivotal. Conservative treatments, including topicalsteroids,vitamins, antioxidants, and physiotherapy, offer symptomatic relief from pain and burning sensation. Intralesional injections of placental extracts, acting through biogenic stimulation based on tissue therapy, are also recommended.[9]

The emergence of lasers (Light Amplification by Stimulated Emission of Radiation) in recent years has garnered attention due to their efficacy in alleviating OSMF symptoms.[9] With advantages such as a bloodless operative field, minimal invasiveness,reduced fibrosis,scarring, and tissue shrinkage post-healing, lasers present a valuable alternative to Low-Level Laser Therapy (LLLT) in OSMF patients.[10] Various staging and grading classification systems have been proposed in medical literature. Passi et al.[11]proposed a comprehensive classification system encompassing clinical and histopathological features, functional components, treatment aspects, and prognosis, offering a holistic approach to OSMF classification. The present study experimentally compared the effects of Low-Level Laser Therapy with Intralesional Injections versus Intralesional Injections alone for the treatment of Grade-II Oral Submucous Fibrosis.

MATERIALANDMETHODS

Data was gathered from patients seeking treatment for Grade- II OSMF at the Outpatient Department (OPD) of the Department of Periodontology at Inderprastha Dental College and Hospital, Sahibabad, Ghaziabad, India. The study comprised 20 individuals diagnosed with OSMF, who were randomly assigned to two treatment groups, with each groupconsisting of 10 patients. Group A (n=10) received treatment solely through Intralesional Injections, while Group B (n=10) underwent a combination therapy of Low-Level Laser Therapy along with Intralesional Injections.

Thestudyincludedpatientsaged17yearsandolder,ofbothgenders. Participantswere required to exhibitgood systemicand mental health without any conditions thatcould potentiallyimpact the effectiveness of the therapy. Additionally, patients had to have Grade II oral submucous fibrosis (OSMF) with a mouth opening ranging from 25 to 35mm, as defined by Passi et al. (2017).[11] Candidates with no known allergies to the materials used in the treatment were included.Finally,individualswillingtoprovideinformedconsentandcapableoffollowing instructions, whether written or verbal, were considered for participation. The exclusion criteria for the study included debilitating systemic or infectious diseases such as HIV or hepatitis, or any conditions affecting the periodontium. Poor compliance or failure to maintain good oral hygiene, as well as the continuation of deleterious habits, were also grounds for exclusion. Additionally, individuals with a known allergy to any of the materials used in the study, pregnant or lactating women, and those who

failed to complete the informed consent process were not considered for participation. Ethical approval to conduct the study was obtained from the institute.

Before the procedure (baseline) and then every two weeks for a total of four weeks, the following parameters were recorded: mouth opening, which was measured using a Digital Vernier Caliper, and burning sensation, which was assessed using a Visual Analogue Scale (VAS). Patients were given oral hygiene instructions. Informed written consent was obtained after explaining the nature of the study.

The patients in Group-A were administered hyaluronidase 1500 IU mixed in 1.5 ml of dexamethasone and 0.5 ml of lignocaine HCL injected intra-lesionally biweekly for 4 weeks. These were diluted in lignocaine to reduce local irritation and ensure better spread. They were administered submucosally over the involved sites using an insulin syringe and needle to minimize the fibrosis caused dueto repeated injection(Figure-1).The patients inGroup-B were given Low Level Laser Therapy along with the Intralesional Injections as given to Group-A patients. (Figure-2) The diode laser unit was set at an output power of 0.8 W and a wavelength of 940nm. Prior to starting with LLLT, the patient was seated comfortably on the dental chair, and both the patient and the operator adorned protective eyewear. Each session consisted of three cycles of low-level laser applications, each lasting for 10-15 seconds, with a gap of approximately 20-30 seconds between each cycle, resulting in a total laser application time of about three minutes. The application of the laser was performed in the non-contact mode, maintaining a distance of 2-3 cm between the laser tip and the fibrous band surface or mucosal surface. The laser beam was applied in a continuous sweeping, circular motion to cover the surfaceof the lesion.Precautions were takento prevent overheating of the mucosa and/or tissue surface, including a 20-30 second gap after each cycle, the continuous sweeping motion of the laser beam, and the 2-3cm distance between the laser tip and the mucosal surface.

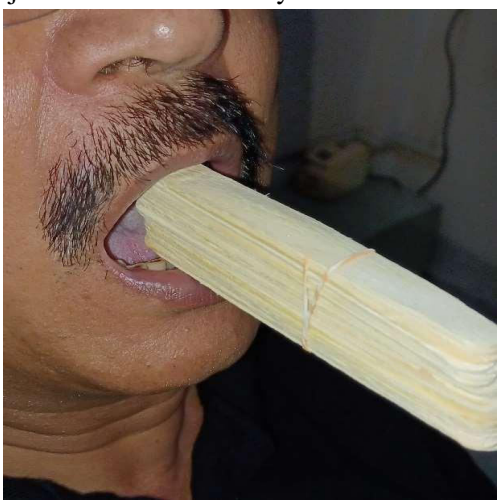
Figure1:Intralesional injections applied on the buccalmucosa

Figure2:Diodelaserapplication(LLLT)on thebuccalmucosa

POSTOPERATIVEINSTRUCTIONSGIVENTOTHEPATIENT-
IMMEDIATE-
Patients were instructed not to rinse their mouth for at least 1 hour after taking the submucosal injections. They were advised to cease any further tobacco abuse in any form. Patients were prescribed carotene and multivitamins.
ATHOME-They were instructed to perform local massage of the oral cavity by placing the middle three fingers in the mouth and the thumb over the cheek to help break the fibrous bands and improve local vascularity.**ICE CREAM STICK EXERCISE-** The patients were advised to place the stack of ice cream sticks in their mouth between the back upper and lower teeth that matched how far they could comfortably open their mouth (Figure-3). They were instructed to add one stick to the current stack to expand the jaw and keep the stack of sticks there for 30-60 seconds, four times a day.

Figure 3: Ice cream stick exercise

The study parameters were subjected to statisticalanalysis.



RESULTS-

Figure4:GroupA-MouthOpeningatBaseline
Figure5:GroupA-Mouth Opening at 4weeks

In terms of mouth opening, during visit 1 and visit 2, the mouth opening in both groups displayed nearly similar values, exhibiting an insignificant variance. (p value- 0.231 and 0.069 respectively). However, from visit 3 to visit 8, the mouth opening in Group-B (Intralesional Injection + LLLT group) was notably greater than that in the Intralesional Injection alone, displaying significant differences (Table-1), (Figure-4 to Figure-7). For pain perception, during visit 1 and the following visits until visit 8, the perception of pain was nearly identical in both groups, indicating an insignificant variance between the groups (Table-2).

Figure6:GroupB-Mouth Opening at Baseline

Figure7:GroupB-Mouth Openingat4weeks

Table1-Inter group comparison of mouthopening(inmm)

Independentttest;*indicates asignificantdifferenceatp≤0.05

Visit	IntralesionalInjection		IntralesionalInjection+LLLT		Difference	p-value
	Mean	SD	Mean	SD		
Visit1	19.44	0.90	20.46	1.51	-1.02	0.231
Visit2	20.12	0.81	21.94	1.76	-1.82	0.069
Visit3	20.82	0.83	23.44	2.09	-2.62	0.032*
Visit4	21.56	0.59	25.04	2.40	-3.48	0.014*
Visit5	22.28	0.61	26.38	2.68	-4.10	0.010*
Visit6	22.96	0.69	28.16	2.56	-5.20	0.002*
Visit7	23.60	0.89	28.00	2.15	-4.40	0.007*
Visit8	24.64	0.88	32.08	3.30	-7.44	0.001*

Table2-Intergroupcomparisonofpain perception (VAS Score)

Visit	IntralesionalInjection		IntralesionalInjection+LLLT		Difference	p-value
	Mean	SD	Mean	SD		
Visit1	8.40	0.55	8.60	0.55	-0.20	0.459
Visit2	8.20	0.45	8.20	0.45	0.00	1.000
Visit3	7.40	0.55	7.40	0.55	0.00	1.000
Visit4	7.20	0.84	7.20	0.45	0.00	0.905
Visit5	6.60	0.89	5.80	0.45	0.80	0.074
Visit6	5.60	0.89	5.40	0.55	0.20	0.403
Visit7	5.60	0.55	5.00	0.71	0.60	0.166
Visit8	4.60	0.55	4.80	0.45	-0.20	0.513

MannWhitneyUtest;*indicatesasignificantdifference atp≤0.05

DISCUSSION

The study compared Intralesional Injection alone versus Intralesional Injection combined with Low-Level Laser Therapy (LLLT) for improving mouth opening over multiple visits. Initially, no significant difference was found between the two groups at visits 1 and 2. However, from visit 3 onwards, the

addition of LLLT showed a notable impact, with consistent statistical significance. Pain perception did not significantly differ between the groups across all visits. Therefore, the study suggests that combining LLLT with Intralesional Injection improvesmouth opening outcomes, offering promise for managing conditions affecting oralfunctionality.

OSMF, initially identified among Indians in 1953, is a chronic and progressive ailment that has been reported in the Indian subcontinent.[11,12] Subsequently, cases were documented inSoutheastAsian and Western countries.[13] Literature surveys indicate varied gender distribution, with some studies noting a female predominance, particularly in India, while others suggest male predominance, possibly linked to the easy accessibility of areca nut and its derivatives.[14] The buccal mucosa and palate are commonly affected sites.

The condition has a multifactorial etiology, with habitual gutkha chewing and other areca nut products playing significant roles. Areca nut is one of the most widely consumed addictive substances, ranking alongside nicotine, ethanol, and caffeine. The nut's constituents, including flavonoids, alkaloids, and copper, disrupt the extracellular matrix's homeostasis. Notably, arecoline, among the alkaloids like guvacine, guvacoline, and arecaidine, is identified as the most potent. These alkaloids stimulate fibroblasts, leading to increased collagen production. Meanwhile, flavonoids such as catechins and tannins are recognized for suppressing collagenase,enhancing collagen cross-linkage, and consequently reducing its degradation.

Inflammation of the oral mucosa triggers T-cell activation and the recruitment of macrophages, resulting in an increased level of pro-inflammatory cytokines and transforming growth factor- beta (TGF-β). The latter significantly boosts collagen production by activating procollagen genes and upregulating procollagen proteinase enzymes, along with the activation of lysyl oxidase.[15] TGF-β also activates the genes of tissue inhibitor of matrix metalloproteinase and plasminogen activator inhibitor, inhibiting collagen degradation. The areca nut, containing a high concentration of copper, stimulates lysyl oxidase, a crucial enzyme for the final cross- linking of collagen.

Fibrosis-induced reduction in blood supply contributestofatigue andextensive degeneration of muscles.[16] Diagnostic criteria encompass a burning sensation in the mouth, ulcer formation (sometimes with vesicles),xerostomia,blanchingoftheoralmucosa,andeventualstiffness.

Palpation reveals fibrotic bands running vertically along the cheek and circumferentially surrounding the lips. Advanced cases exhibit blanching of the oral mucosa, limited soft palate movement, and a shrunken uvula, along with restricted tongue movements.[16]

Administering intralesional injections containing hydrocortisone, placental extract, hyaluronidase, and triamcinolone, coupled with oral intake of iron supplements, antioxidants, and vitamins, has demonstrated effectiveness in managing early-stage cases. Surgical intervention, involving the excision of fibrotic bands followed by secondary intention healing,is considered appropriate only for moderately advanced and advanced cases. However, several reports indicate that this surgical approach may potentially exacerbate fibrosis and disability, causing increased overall discomfort for the patient. According to Leena et al,[17] patients treated with hyaluronidase experienced a rapid reduction in the burning sensation. However, the combined long-term effects of dexamethasone and hyaluronidase were found to be more significant than other management modalities. While dexamethasone comes with its own advantages and contraindications, the results observed in combination with hyaluronidase are more promising.

Carcinogensfromthearecanutaccumulatebeneaththeepithelium,leadingtoreduced vascularityandthe swift penetration of carcinogensintothesystemiccirculation.Conservative treatments,s uchastopicalsteroids,vitamins,antioxidants,andphysiotherapy,offer symptomaticrelief.[18]Intralesionalinjectionofplacentalextractsemergesasapreferable alternativetohyaluronidase,actingthroughbiogenicstimulationoftissue.Contrarytothe postulation by Borle and Borle[19] that intralesional injections of multiple drugs may worsen the existing condition, our study

did not find this to be the case, as follow-up was not conducted.
Theconditiondeterioratеswithmultipleinjections,attributedtorepeatedneedlestickinjuries and clinical irritation from medications.[20]

Following numerous clinical trials, glucocorticoids such as hydrocortisone, triamcinolone, betamethasone, and dexamethasone have demonstrated minimal effectiveness in relieving symptoms. They exert their impact through anti-inflammatory activity and the promotion of apoptosis. Steroids prove useful in symptom minimization or as adjunct therapy. On the other hand, hyaluronidase, an enzyme, can accelerate OSF by depolymerizing hyaluronic acid, thereby reducing viscosity and diminishing collagen formation.[20]
Pentoxifylline is employed for its vasodilating properties and its ability to decrease blood viscosity.[21] Gupta et al. discovered that a six-week treatment with tablets containing carotene and vitamin E yielded effective outcomes.[22] Additionally, antioxidants like vitamin E and lycopenewere administered,enhancingresultsthreefold.Itisnoteworthythatnosingle drugshas proven to be entirely effective in managing OSMF. The pathogenicity of OSMF remains unclear, and the options for administration are limited.[23]
In the contemporary era marked by advanced science and technology, the use of lasers for alleviating fibrotic bands holds the potential for faster healing and minimal scarring. Diode lasers, characterized by their compact and portable nature, find numerous applications in the medical field. The active component in a semi-conducting diode laser is gallium arsenide or similar compounds. Laser technology enables the sealing of blood vessels smaller than 0.5 mm in diameter, contributing to exceptional visibility and precision during treatment.
The laser beam is transmitted through an optical fiber delivery system, with the tissue cutting depth being less than 0.01 mm. This preserves structures beyond this depth, causing minimal damage to adjacent tissues. Another advantage is that lasers create a coagulum of denatured proteins on the tissue surface, acting as a dressing in the treated site.
While lasers are not a universal remedy for treating OSMF, they offer a simple, patient- and surgeon-friendly procedure with effective results.[23] Further studies involving a largerpopulation and additional parameters are necessary to arrive at a comprehensive conclusion. In cases of OSMF, collagen production is increased while collagen degeneration is decreased. Administering hyaluronidase and dexamethasone on the lesion has proven to be an efficient approach in handling OSMF, potentially eradicating the complications linked with surgical intervention.

CONCLUSION

This research represents an additional initiative to furnish evidence-based backing for refining patient care. The results of the present study support the fact that laser treatment along-with intralesional injections is an acceptable treatment modality for OSMF patients.

ACKNOWLEDGMENT

No external funding, apart from the support of the authors' institution, was provided for this study.

REFERENCES

1. MehrotraD, KumarS,AgarwalGG, AsthanaA,KumarS.Oddsratioofrisk factors for oral submucous fibrosis in a case control model. Br J Oral Maxillofac Surg. 2013 Oct;51(7):e169-73.
2. Wollina U, Verma SB, Ali FM, Patil K. Oral submucous fibrosis: an update. Clin Cosmet Invest Dermatol.2005;8:193–204.
3. Pindborg JJ, Sirasat SM. Oral submucous fibrosis. Oral Surg Oral Med Oral Pathol. 1966;22:746–779.
4. Gondivkar SM, Bhowate RR, Gadbail AR, Sarode SC, Patil S. Quality of life and oral potentially malignant disorders: Critical appraisal and prospects. World J Clin Oncol. 2018 Aug 13;9(4):56-59.

5. Angadi PV, Rao S. Management of oral submucous fibrosis: an overview. Oral Maxillofac Surg. 2010;14:133–142.
6. Chole RH, Gondivkar SM, Gadbail AR, Balsaraf S, Chaudhary S et al. Review of drug treatment of oral submucous fibrosis. Oral Oncol. 2012 May;48(5):393-8.
7. Singh M, Niranjan HS, Mehrotra R, Sharma D, Gupta SC. Efficacy of hydrocortisone acetate/hyaluronidase vs triamcinolone acetonide/hyaluronidase in the treatment of oral submucous fibrosis. Indian J Med Res. 2010;131:665–669
8. Shah A, Raj S, Rasaniya V, Patel S, Vakade M. Surgical management of oralsubmucous fibrosis with the ‘‘Opus-5’’ Diode laser. J Oral Laser Appl. 2005;5:37–43.
9. Chandra S, Gujjari SK, Sankar AR. Biostimulation with diode lasers: A novel futuristic approach in the treatment of oral submucous fibrosis – A case report. Int J Med Dent Case Rep 2019;6:1-4.
10. Passi D, Bhanot P, Kacker D, Chahal D, Atri M, Panwar Y. Oral submucous fibrosis: Newer proposed classification with critical updates in pathogenesis and management strategies. Natl J Maxillofac Surg 2017;8:89-94.
11. Joshi SG. Submucous fibrosis of the palate and pillars. Indian J Otolaryngol1953;4:1-4.
12. Gupta PC, Sinor PN, Bhonsle RB, Pawar VS, Mehta HC. Oral submucous fibrosis in India: A new epidemic? Natl Med J India 1998;11:113-6.
13. Murti PR, Gupta PC, Bhonsle RB, Daftary DK, Mehta FS, Pindborg JJ. Effect on the incidenceoforalsubmucousfibrosisofinterventionintheareca nutchewinghabit. JOral Pathol Med 1990;19:99-100.
14. Lokesh U, Veena GC, Jannu A, Vivek GK, Shilpa MR. Application of lasers for oral submucus fibrosis-an experimental study. Arch CranOrofac Sci 2014;1:81-6.
15. Canniff JP, Harvey W, Harris M. Oral submucous fibrosis: Its pathogenesis and management. Br Dent J 1986;160:429-34.
16. Jame L, Shetty A, Rishi D, Abraham M. Management of oral submucous fibrosis with injection of hyaluronidase and dexamethasone in grade III oral submucous fibrosis: a retrospective study. J Int Oral Health 2015;7(8):82–85.
17. Tekade SA, Chaudhary MS, Tekade SS, Sarode SC, Wanjari SP, Gadbail AR, et al. Early stage oral submucous fibrosis is characterized by increased vascularity asopposed to advanced stages. J Clin Diagnos Res 2017;11(5):92–96.
18. Borle RM, BorleSR.Management of oral submucousfibrosis: a conservativeapproach. J Oral Maxillofac Surg 1991;49(8):788–791.
19. Sinha SN, Jain PK. Intraoral injection of hydrocortisone and placental extract in oral submucous fibrosis. Indian J Otolaryngol 1978;30(2):103.
20. Jiang X, Hu J. Drug treatment of oral submucous fibrosis: a review of the literature. J Oral Maxillofac Surg 2009;67(7):1510–1515.
21. Gupta S, Reddy MVR, Harinath BC. Role of oxidative stress and antioxidants in aetiopathogenesis and management of oral submucous fibrosis. Indian J Clin Biochem2004;19(1):138.
22. Singh D, Padshetty S. Injection placentrex in the management of oral submucous fibrosis. Int J Mod Sci Eng Technol 2015;2(1):23–30.
23. Warnakulasuriya S, Kerr AR. Oral Submucous fibrosis: a review of the current management and possible directions for novel therapies. Oral Surg, Oral Med, Oral Pathol Oral Radiol 2016;122(2):232–241.