ORIGINAL RESEARCH

# Comparative Evaluation of Low-level Laser Therapy and Intralesional Injection in OSMF Patients: A Quasi-randomized Trial

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## Abstract

**Aim:** The aim of the present study was to compare the effectiveness of low-level laser therapy and intralesional injection in oral submucous fibrosis (OSMF) patients.

**Materials and methods:** The present study comprised of 52 grade II OSMF patients aged between 20 and 60 years. A pretreatment assessment was done for each patients. And 52 patients were divided into two groups (26 patients in each group). Group I received intralesional injections, and group II received low-level laser therapy (LLLT). The intralesional injection group received 0.5 mL 1500 I.U. Hyaluronidase with 2 mL dexamethasone biweekly for a month. The LLLT group underwent sessions of 0.1 watt laser only once for 3 cycles, each lasting 1 minute with 5-minute intervals. Evaluation of overall accessibility, burning sensation and mouth opening was done for both the treatment modalities on 0, 3rd, 7th and 15th day. All data were recorded and statistically analyzed.

**Results:** On comparison of burning sensation in intralesional Injection group, at baseline, the mean value was $4.00 \pm 0.84$ and it reduced to $1.19 \pm 0.40$ while in LLLT group from $4.15 \pm 0.96$ at baseline, it reduced to $2.65 \pm 0.68$ at the end of 15 days, respectively. On comparison of mouth opening in intralesional Injection group, at baseline, the mean value was $21.73 \pm 1.56$ and it increased to $32.53 \pm 0.97$ while in LLLT group from $22.70 \pm 2.17$ at baseline, it increased to $24.50 \pm 1.31$ at the end of 15 days, respectively. There was a statistically significant difference found between the two groups.

**Conclusion:** The present study concluded that intralesional injections are more effective in treating grade II OSMF compared with LLLT.

**Clinical significance:** Several different treatment options are available to treat OSMF, including medical approaches, surgical management, and physiotherapy. One of the important therapeutic modalities is intralesional injection therapy with corticosteroids as they reduce inflammation and immunosuppression while hyaluronidase increases tissue permeability.

**Keywords:** Fibrosis, Intralesional injections, Laser therapy, OSMF grade II.

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## Introduction

One of India's greatest doctors, Sushruta, was known to refer to oral submucous fibrosis (OSMF) as "Vidari."[1] Constant chewing of areca nut and its products causes hyperactivity of masticatory muscles, the glycogen stores to be depleted, and the muscles to become fatigued. After fibrosis, the muscles experience severe degeneration and fibrosis due to the diminished blood flow, which exacerbates muscular fatigue. [2]

As the disease progresses, white, opaque fibrous bands appear with blanched oral mucosa. The condition is usually symmetrical, with vertical fibrous bands in the buccal mucosa. The overall prevalence of OSMF is about 4.47% worldwide and 6.36% in India. In India, oral cancer occurs at a high rate of 20 cases per 1,00,000 people, making up more than 30% of all cancer cases in the country.[3]

Several different treatment options are available to treat this illness, including medical approaches, surgical management, and physiotherapy. Intralesional corticosteroid injections with hyaluronidase remain standard, as corticosteroids reduce inflammation and immunosuppression while hyaluronidase increases tissue permeability. Hence, they help in increasing mouth opening.[4] Low-level laser therapy (LLLT), or soft laser treatment, uses a device with an output of 0.1–0.6 watts and is highly effective.[5] Low-level laser therapy offers benefits over traditional tissue

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regeneration methods, such as improved inflammatory response, reduced edema, and pain relief.[6] It stimulates fibroblast growth, influencing fibroblast development and motility, and is effective at low doses. Very limited studies were available on the comparison of the LLLT and intralesional injection treatment modalities. Hence, the present study was conducted to compare the LLLT and intralesional injection as a treatment modality in OSMF grade II patients and also to compare the treatment outcomes between both the treatment modalities based on accessibility, burning sensation and mouth opening.

## Materials and Methods

The present quasi-randomized trial study was conducted in the Department of Oral and Maxillofacial Surgery, Kalinga Institute of Dental Sciences, Bhubaneswar, Odisha, from April 2022 to February 2024. Patients including males and females aged 20–60 years with OSMF grade II, patients who were not taking any medications for OSMF previously and willing to participate in the study were included in the present study. Patients with OSMF grades I and III, undergoing OSMF treatment, coagulopathies, blood disorders, Parkinson's, heart disease, and those unwilling to participate were excluded from the study. Patient histories and tobacco habits were documented and before the clinical procedures, patients were advised to stop these habits. Ethical clearance was obtained, and patients received treatment information and consent forms. Demographic data and signed consent were recorded. Haider et al. Classification system (2000)[7] of OSMF patients was considered for this study:

Pretreatment assessments were done before group allocation as follows.

Accessibility: The presence of facial and buccal bands was assessed clinically by palpation method. Reduction in bands was noted as increased accessibility. Corresponding increase in mouth opening was also noted as increased accessibility. *Burning sensation:* VAS scale was used for scoring. The scoring system was marked between 1 and 10 as on the scale. A decreased score on the scale showed the efficacy of the treatment. *Mouth opening:* An electronic carbon fiber vernier caliper gauge (ToolsCentre™, Generic LSHAZI03590). The inter-incisal distance between upper and lower central incisors was measured. Average normal mouth opening = 35–55 mm.

A total of 52 patients with OSMF grade II were divided into two groups of 26. Group 1 received intralesional injections, and group II received LLLT.

*Group I:* Intralesional Injections: The palpable bands received injections: Hyaluronidase (Hynidase and Dexona) (1500 I.U. diluted with 1 mL sterile water and 2% Lignocaine with 1:200000 Adrenaline, 0.5 mL injected biweekly) and Dexamethasone (2 mL biweekly for 1 month) (Fig. 1).

*Group II:* Low-level laser therapy (LLLT): Isolated mucosal areas exhibiting palpable bands were subjected to laser biostimulation (Biolase diode laser). Prior to the therapy, protective eyewear was advised to be worn by the doctor, assistant, and patient. A diode laser was used for this study of wavelength 980 nm and an output power of 0.1 W. The LLLT is given only once for three cycles of with each cycle for 1 min duration with a gap of 5 minutes between each cycle. Laser biostimulation was applied over the affected surface in contact mode in a continuous sweeping motion over the affected surface (Fig. 2).

**Fig. 1:** Administration of intralesional injections

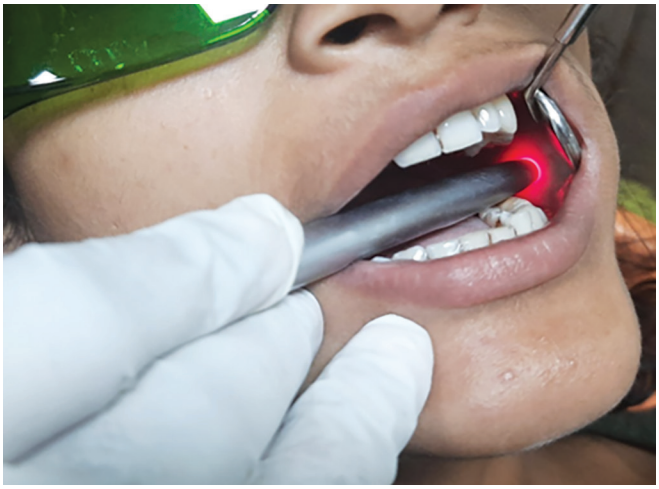

**Fig. 2:** Laser biostimulation

Evaluation of overall accessibility, burning sensation, and mouth opening was done for both the treatment modalities on 0, 3rd, 7th and 15th day.

### Statistical Analysis

Data analysis was done by SPSS® version 24.0 and Chi-square and Wilcoxon tests were used to analyze the data. The significance was assessed at a 5% level of significance with a 95% confidence interval.

## Results

A quasi-randomized trial was conducted on the 52 grade II OSMF patients aged between 20 and 60 years. The mean age of group I was 34.2 years and group II was 38.3 years. About 42 males and 10 females were included in the present study. Table 1 and Figure 3 show the intragroup comparison of access at different follow-up points. For intralesional injection group, the accessibility was increased from 34.6% at baseline to 88.5% on 15th day. A statistically significant difference was found between baseline to 7th day.

**Table 1:** Intragroup comparison of accessibility at different follow-up points in intralesional injection group

| *Follow-up days* | *At day 0* | | *At day 3* | | *At day 7* | | *At day 15* | |
|---|---|---|---|---|---|---|---|---|
| | *n* | *%* | *N* | *%* | *N* | *%* | *n* | *%* |
| Not present/ reduced | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Present | 17 | 65.4 | 14 | 53.8 | 9 | 34.6 | 3 | 11.5 |
| Increased | 9 | 34.6 | 12 | 46.2 | 17 | 65.4 | 23 | 88.5 |
| *p*-value | Day 0 * day 3 – 0.250, NS<br>Day 0 * day 7 – 0.008, S<br>Day 0 * day 15 – <0.001, S | | | | | | | |

S, significant; NS, non-significant

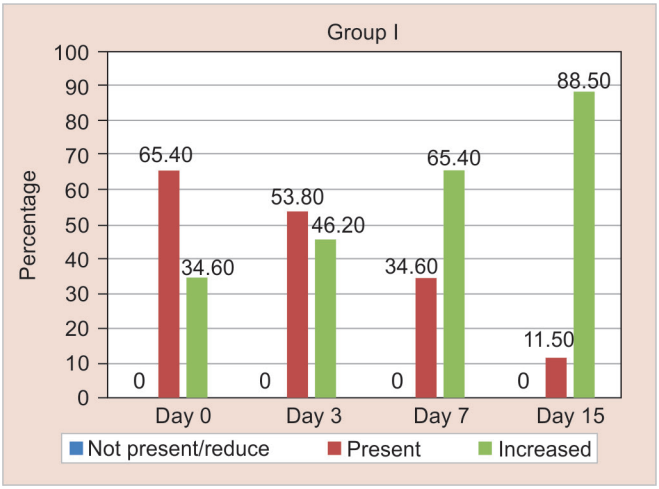


**Fig 3:** Intragroup comparison of access at different follow-up points in intralesional injection group

**Table 2:** Intragroup comparison of accessibility at different follow-up points in low-level laser therapy group

| *Follow-up days* | *At day 0* | | *At day 3* | | *At day 7* | | *At day 15* | |
|---|---|---|---|---|---|---|---|---|
| | *n* | *%* | *N* | *%* | *N* | *%* | *n* | *%* |
| Not present/ reduced | 5 | 19.2 | 5 | 19.2 | 0 | 0 | 0 | 0 |
| Present | 21 | 80.8 | 21 | 80.8 | 26 | 100 | 26 | 100 |
| Increased | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| *p*-value | Day 0 * day 3 – 1.000, NS<br>Day 0 * day 7 – 0.234, NS<br>Day 0 * day 15 – 0.234, NS | | | | | | | |

NS, non-significant

Table 2 and Figure 4 show the intragroup comparison of access at different follow-up points. In LLLT group, the accessibility was increased from 80.8% at baseline to 100% on 15th day. However, there was no significant difference found between different intervals.

On comparison of burning sensation in intralesional injection group, at baseline, the mean value was 4.00 ± 0.84 and it reduced to 1.19 ± 0.40 while in LLLT group from 4.15 ± 0.96 at baseline, it reduced to 2.65 ± 0.68 at the end of 15 days respectively (Tables 3 and 4 and Figs 5 and 6) On comparison of mouth opening in intralesional injection group, at baseline, the mean value was

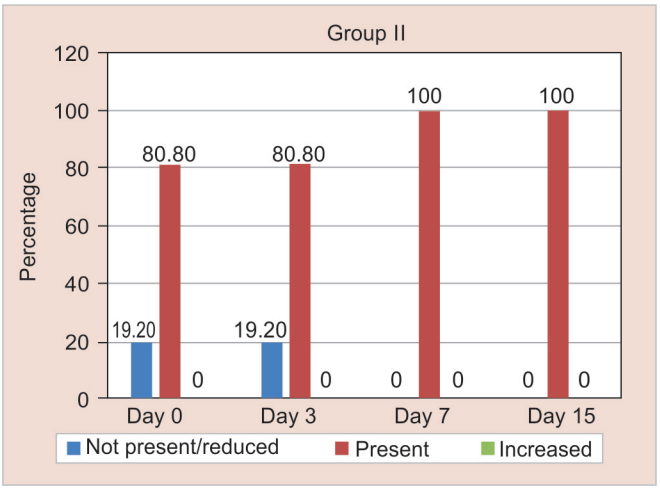


**Fig. 4:** Intragroup comparison of access at different follow–up points in low-level laser therapy group

**Table 3:** Intragroup comparison of burning (VAS) at different follow-up points in intralesional injection group

| *Follow-up days* | *N* | *Minimum* | *Maximum* | *Mean* | *Std. Deviation* |
|---|---|---|---|---|---|
| At day 0 | 26 | 3.00 | 5.00 | 4.0000 | 0.84853 |
| At day 3 | 26 | 2.00 | 5.00 | 3.4231 | 1.06482 |
| At day 7 | 26 | 1.00 | 3.00 | 2.1538 | 0.67482 |
| At day 15 | 26 | 1.00 | 2.00 | 1.1923 | 0.40192 |
| *p*-value | <0.001, S | | | | |
| *Post hoc* pairwise comparison | Day 0 * day 3 – <0.001, S<br>Day 0 * day 7 – <0.001, S<br>Day 0 * day15 – <0.001, S | | | | |

S, significant

**Table 4:** Intragroup comparison of burning (VAS) at different follow-up points in low-level laser therapy group

| *Follow-up days* | *N* | *Minimum* | *Maximum* | *Mean* | *Std. deviation* |
|---|---|---|---|---|---|
| At day 0 | 26 | 3.00 | 6.00 | 4.1538 | 0.96715 |
| At day 3 | 26 | 3.00 | 4.00 | 3.6154 | 0.49614 |
| At day 7 | 26 | 3.00 | 4.00 | 3.3077 | 0.47068 |
| At day 15 | 26 | 2.00 | 4.00 | 2.6538 | 0.68948 |
| *p*-value | <0.001, S | | | | |
| *Post hoc* pairwise comparison | Day 0 * day 3 – 0.002, S<br>Day 0 * day 7 – 0.003, S<br>Day 0 * day15 – <0.001, S | | | | |

S, significant

21.73 ± 1.56 and it increased to 32.53 ± 0.97 while in LLLT group from 22.70 ± 2.17 at baseline, it increased to 24.50 ± 1.31 at the end of 15 days respectively (Tables 5 and 6 and Figs 7 and 8). *Post hoc* pairwise comparison reveals there was a significant difference found between day 0 vs day 3, day 0 vs day 7 and day 0 vs day 15 ($p < 0.001$).

The inference of the present study indicated that the intralesional injection of hyaluronidase with dexamethasone is a faster and standard treatment of grade II OSMF than low-level laser stimulation.

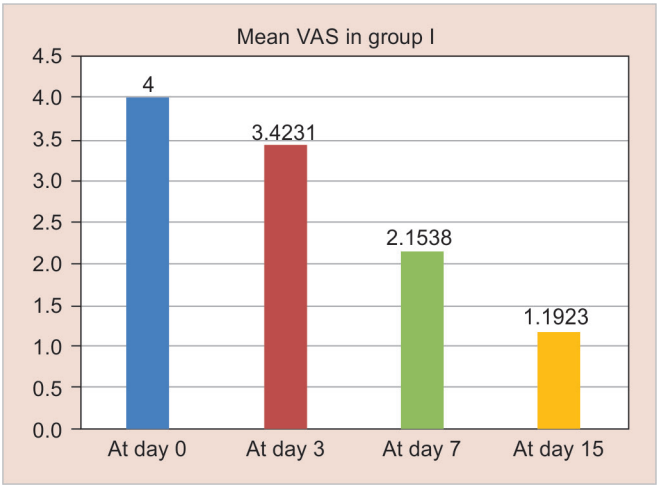


**Fig. 5:** Intragroup comparison of burning (VAS) at different follow up points in intralesional injection group

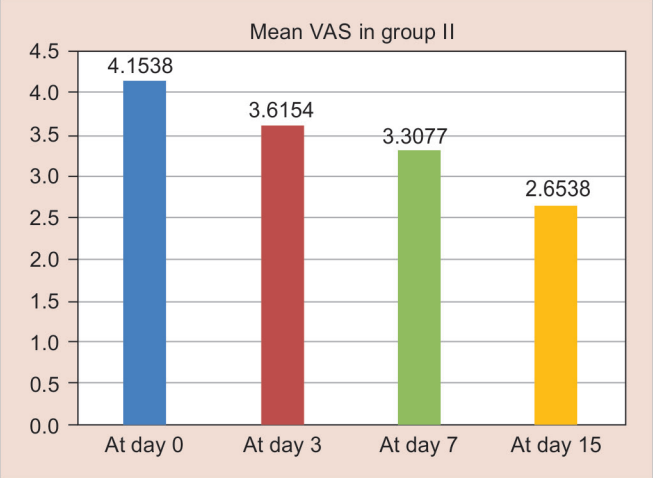


**Fig. 6:** Intragroup comparison of burning (vas) at different follow-up points in low-level laser therapy group

**Table 5:** Intragroup comparison of mouth opening at different follow-up points in intralesional injection group

| *Follow-up days* | *N* | *Minimum* | *Maximum* | *Mean* | *Std. deviation* |
|---|---|---|---|---|---|
| At day 0 | 26 | 19.00 | 24.00 | 21.7338 | 1.56587 |
| At day 3 | 26 | 22.00 | 26.00 | 24.1731 | 1.14841 |
| At day 7 | 26 | 26.30 | 30.69 | 27.9865 | 1.34276 |
| At day 15 | 26 | 31.00 | 34.00 | 32.5338 | 0.97372 |
| *p*-value | | | <0.001, S | | |
| *Post hoc* pairwise comparison | | | Day 0 * day 3 – <0.001, S<br>Day 0 * day 7 – <0.001, S<br>Day 0 * day15 – <0.001, S | | |

S, significant

**Table 6:** Intragroup comparison of mouth opening at different follow-up points in low-level laser therapy group

| *Follow-up days* | *N* | *Minimum* | *Maximum* | *Mean* | *Std. deviation* |
|---|---|---|---|---|---|
| At day 0 | 26 | 20.09 | 26.40 | 22.7019 | 2.17872 |
| At day 3 | 26 | 21.00 | 26.90 | 23.4077 | 1.90093 |
| At day 7 | 26 | 22.90 | 26.90 | 24.2519 | 1.36909 |
| At day 15 | 26 | 23.00 | 26.90 | 24.5077 | 1.31816 |
| *p*-value | | | <0.001, S | | |
| *Post hoc* pairwise comparison | | | Day0 * day 3 – <0.001, S<br>Day0 * day 7 – <0.001, S<br>Day0 * day15 – <0.001, S | | |

S, significant

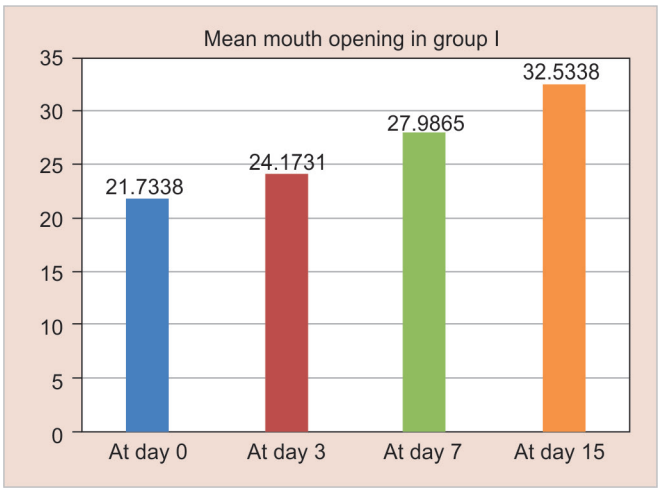


**Fig. 7:** Intragroup comparison of mouth opening at different follow up points in intralesional injection group

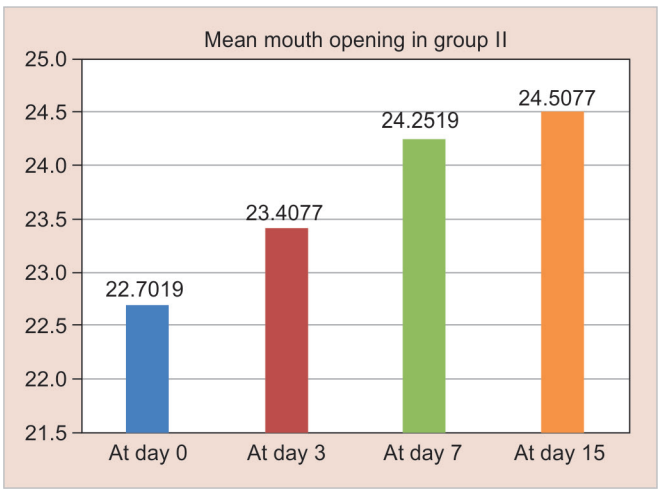


**Fig. 8:** Intragroup comparison of mouth opening at different follow up points in low-level laser therapy group

## Discussion

Oral submucosal fibrosis is considered a potentially malignant disorder of the oral cavity because of its ability to transform into a malignant condition. Various characteristics are evident in a patient with grade II OSMF. Apart from reduced mouth opening, a patient usually reports to the doctor due to a burning sensation over the oral mucosa, eruption of ulcerations, and stiffness of mucosa. This stage of disease progression is slow-growing and is always associated with a synergistic agent *Areca catechu* being the most common synergistic agent which aids in worsening of the symptoms. Various genetic mutations, nutritional deficiencies,

along with any persistent trauma to the oral mucosa aided by the use of tobacco and its products are responsible for the disease to occur and progress into advanced stages.[8]

Early detection, cessation of harmful habits, and prompt treatment can prevent disease progression and alleviate symptoms. Regular follow-ups are crucial for the early detection of malignant transformations. Eliminating contributing factors, such as tobacco use and oral trauma from sharp teeth, is essential. Patients should be encouraged to consume antioxidant-rich foods and supplements to improve symptoms. Literature suggests that intralesional hyaluronidase have been proven to yield faster results in providing relief for burning sensation. It has also been seen that hyaluronidase when combined with dexamethasone provides better results in the long run.[9]

Studies have also been suggestive of multiple injection pricks for the administration of multiple drugs to the lesion sites can induce fibrosis in that area. In the present study, a combination of 0.5 mL of 1500 I.U. of hyaluronidase with 2 mL of dexamethasone has been used in one of the groups. The treatment modality was advocated for 1 month, and the patients received the required dosage twice a week. Hyaluronidase breaks down the ground substance hyaluronic acid of the connective tissue. It has also been reported that it aids in collagen degradation, hence reducing fibrosis and thereby improving the symptoms. Dexamethasone being a steroid, has anti-inflammatory properties along with anti-fibrotic properties. It provides immediate relief to the symptoms along with inhibition of collagen production and deposition. So, the combination of hyaluronidase and dexamethasone work in a synchronized way to prevent fibrosis and provide relief to the symptoms.

In the present study, intralesional injection was better compared with the LLLT. Similarly, a study done by Saalim M et al.[10] stated that betamethasone and hyaluronidase can be considered an efficient option for the reduction of symptoms in OSMF patients as intralesional injections. Guna TP et al.[11] reported similar to the present study results that Injecting hyaluronidase together with dexamethasone is a useful way to manage and get rid of the morbidity in OSMF, while effectively relieving the symptoms. Corticosteroids reduce inflammation and immunosuppression while hyaluronidase increases tissue permeability.

Low-level laser therapy (630–980 nm, 50–500 mw) modulates tissue response, prevents charring, and promotes healing by interacting with Cytochrome C oxidase, reducing pro-inflammatory cytokines, and providing analgesic and anti-inflammatory effects.

The present LLLT group also shows improvement in mouth opening and burning sensation. Similarly, a study conducted by Chandra S et al.[12] mentioned that in a patient with a complaint of reduced mouth opening and burning sensation in the mucosa who underwent LLLT, desirable results were obtained. The results extracted from the study were improvement in mouth opening along with the reduction in burning sensation. Similarly, another study done by Sukanya D et al.[13] stated that the LLLT was used in patients having OSMF. It was concluded that mouth opening was increased in individuals receiving the treatment post-treatment. Hence, this study confirms that LLLT can be used as a treatment modality for OSMF.

Another similar result obtained by Nikita N Burde and Gayathri S[14], showed a patient's mouth opening that improved from 15 to 18 mm with pharmacological therapy, then to 26 mm after trans buccal horizontal incisions using a 980 mm Diode laser was made to release the bands.

According to Aparna TY et al.[15] study subjects with LLLT showed immediate improvement in mouth opening and intralesional injections yielding better long-term results, concluding that both methods are effective, with injections being more beneficial over time, these results are similar to the present study results.

In the present study, the intralesional injection group showed increased access, reduced mouth burning, and improved mouth opening. The procedure time was uniform. In the LLLT group, access remained unchanged, mouth burning decreased and mouth opening improved.

The limitation of the present study is that the present results face scrutiny due to the small sample size. Another challenge to the interpretation of the results has been drawn from the fact that the patients received one full month of treatment whereas the study design planned for recording of results midway during the treatment. However, since it was postulated that maximum efficacy would be noted around the mid-treatment, the study design attempted to record it instead of at treatment completion. However, a large-scale study with complete treatment regimen recording and further analyses should be conducted with a standardized treatment protocol.

## Conclusion

In conclusion, it can be inferred from the study that intralesional injection of hyaluronidase with dexamethasone is a faster and standard treatment of grade II OSMF compared with low-level laser stimulation. So, large-scale studies are required to investigate the higher efficacy and unknown effects of lasers.

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