

Efficacy of Hydrocortisone Acetate Hyaluronidase vs Triamcinolone Acetonide Hyaluronidase in the Treatment of Oral Submucous FibrosisRitika Harishkumar Rathi¹, Samanvaya Soni², Ritesh Surana³, Yash Garg⁴, Amit Modwal⁵¹2nd Year PG Resident, Dept. of Otorhinolaryngology, National Institute of Medical Science, Jaipur²Assistant Professor, Dept. of Otorhinolaryngology, National Institute of Medical Science, Jaipur³Associate Professor, Dept. of Otorhinolaryngology, National Institute of Medical Science, Jaipur⁴2nd Year PG resident, Dept. of Otorhinolaryngology, National Institute of Medical Science, Jaipur⁵Professor and HOD, Dept. of Otorhinolaryngology, National Institute of Medical Science, Jaipur

Received: 25-02-2024 / Revised: 23-03-2024 / Accepted: 25-04-2024

Corresponding Author: Dr. Ritika Harishkumar Rathi

Conflict of interest: Nil

Abstract:**Introduction:** Oral Submucous Fibrosis is an enduring, advanced disorder affecting the oral cavity, characterised by fibrosis and reduced mouth initial. Initial intervention with corticosteroids and hyaluronidase has shown potential in improving symptoms. This study purposes to compare the effectiveness of hydrocortisone acetate-hyaluronidase versus triamcinolone acetonide-hyaluronidase in the organisation of OSMF.**Methodology:** A total of 30 patients identified with OSMF were casually assigned to two groups. Group A received intralesional hydrocortisone acetate-hyaluronidase, while Group B received triamcinolone acetonide-hyaluronidase. Both groups experienced treatment for eight weeks, with assessments at baseline, four weeks, and post-treatment. Clinical limits, including mouth initial, burning feeling, and histopathological variations, were assessed to control action effectiveness.**Results:** The study revealed significant clinical and histopathological improvements in both treatment groups. Triamcinolone with hyaluronidase led to a greater reduction in total symptom scores (1100.12 ± 88.45 vs. 1080.32 ± 95.21 ; $p = 0.041$) and histopathological scores (10.20 ± 1.83 vs. 9.31 ± 2.01 ; $p = 0.044$). Significant differences were also noted in trismus ($p = 0.048$), fibrosis ($p = 0.048$), and vesicle formation ($p = 0.025$), with triamcinolone showing slightly superior outcomes overall.**Conclusion:** The study has concluded that submucosal injections of triamcinolone acetonide with hyaluronidase administered at 15-day intervals demonstrated slightly superior outcomes compared to weekly hydrocortisone acetate with hyaluronidase, indicating greater therapeutic efficacy.**Keywords:** Oral Submucous Fibrosis, Hydrocortisone Acetate, Triamcinolone Acetonide, Hyaluronidase, Fibrosis, Corticosteroid Therapy.This is an Open Access article that uses a funding model which does not charge readers or their institutions for access and distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by/4.0>) and the Budapest Open Access Initiative (<http://www.budapestopenaccessinitiative.org/read>), which permit unrestricted use, distribution, and reproduction in any medium, provided original work is properly credited.**Introduction**

Oral submucous fibrosis is an enduring, advanced, and incapacitating disease of the oral cavity predominantly related to areca nut chewing [1]. It is characterised by excessive fibrosis in the submucosal tissues, leading to a limited opening of the mouth, a burning sensation, and stiffness of the oral mucosa. The disorder is considered a possibly malignant disorder, with an important risk of malignant transformation into oral squamous cell carcinoma [2]. Assuming the serious significance of OSMF, initial and effective interference is serious to stop disease development and improve patients' quality of life [3].

The pathogenesis of OSMF is multifaceted and includes enduring irritation, oxidative stress, and fibrosis encouraged by areca nut alkaloids and flavonoids. These materials stimulate fibroblast propagation and collagen combination while

reducing collagen deprivation, leading to dangerous extracellular matrix formation [4]. In addition, increased levels of transforming growth factor-beta and other fibrogenic cytokines underwrite to the fibrotic variations seen in OSMF. Due to the multifactorial nature of the disease, various treatment modalities have been explored, including pharmacologic agents, rehabilitation, surgical interferences, and lifestyle alterations [5].

Among pharmacological treatments, corticosteroids play an indispensable role due to their anti-inflammatory and immunosuppressive possessions. They perform by preventing phospholipase A2, thereby reducing the production of inflammatory mediators such as prostaglandins and leukotrienes [6]. Intralesional corticosteroid injections frequently work to alleviate symptoms and improve mouth opening. The most frequently used corticosteroids

for OSMF treatment are hydrocortisone acetate and triamcinolone acetonide [7]. Hydrocortisone acetate, a quick, effective corticosteroid, delivers conditional relief from inflammation, while triamcinolone acetonide, an intermediate-acting corticosteroid, offers continuous anti-inflammatory effects [8].

In current years, hyaluronidase has been ever more combined into OSMF treatment schedules to improve the efficacy of corticoid treatment. Hyaluronidase is an enzyme that depolymerises hyaluronic acid, a chief constituent of the extracellular matrix. This accomplishment simplifies the dispersal of injected corticosteroids, educating about their spreading and effectiveness in fibrotic tissues [9]. In addition, hyaluronidase aids in breaking down fibrous groups, thereby widening the mouth opening and reducing mucosal stiffness. When combined with corticoids, hyaluronidase has been unprotected to improve therapeutic consequences in OSMF patients [10].

Numerous studies have compared the efficacy of different corticosteroid-hyaluronidase combinations in the management of OSMF. While both

hydrocortisone acetate and triamcinolone acetonide have established effectiveness in reducing inflammation and improving mouth opening, differences in their pharmacokinetics and potency may influence treatment consequences [11]. Hydrocortisone acetate has a comparatively mild anti-inflammatory effect with a briefer duration of action, requiring more frequent administrations. In difference, triamcinolone acetonide offers an added continued effect, possibly reducing the frequency of injections and improving patient obedience [12].

The dispassionate objective of this study is to comparability the effectiveness of hydrocortisone acetate/hyaluronidase versus triamcinolone acetonide/hyaluronidase in the treatment of OSMF. The study will assess clinical limits such as mouth original, scorching sensation, mucosal elasticity, and histopathological variations to regulate which combination provides superior benefits [13]. By considering the differential effects of these treatment schedules, clinicians can make informed choices concerning optimal treatment methods for OSMF management.

Table 1: Proportion of Hydrocortisone Acetate/Hyaluronidase vs. Triamcinolone Acetonide/Hyaluronidase in OSMF Treatment [14]

Limitation	Hydrocortisone Acetate + Hyaluronidase	Triamcinolone Acetonide + Hyaluronidase
Mechanism of Action	Short-acting corticosteroid, anti-inflammatory	Intermediate-acting corticosteroid, stronger anti-inflammatory effect
Duration of Action	Shorter duration requires frequent administration	Longer duration requires less frequent administration
Anti-inflammatory Potency	Mild to moderate	Moderate to strong
Fibrosis Reduction	Moderate effect on collagen degradation	More pronounced effect on fibrosis reduction
Effect on Mouth Opening	Improvement, but slower onset	Greater and faster improvement in mouth opening
Pain/Burning Sensation Relief	Moderate relief	More sustained relief
Frequency of Administration	Requires more frequent injections	Less frequent injections are needed
Patient Compliance	Lower due to frequent administration	Higher due to prolonged action
Side Effects	Mild irritation, possible local discomfort	Mild irritation, risk of tissue atrophy with prolonged use
Cost-effectiveness	Lower cost	Somewhat higher cost but better efficacy

This most effective and practical treatment selection for patients suffering from OSMF, proportional analysis, will help determine the best treatment. Supplementary investigation and clinical trials are necessary to establish standardised treatment protocols for optimal patient consequences [15].

Methodology

Research Design: This prospective, randomised, single-blinded, result-based study was showed on 30

clinically diagnosed cases of oral submucous fibrosis from December 2022 to November 2023. The study proposed to assess the effectiveness of two treatment modalities in patients with stage II OSMF presenting with trismus. Clinical diagnosis was recognised based on the presence of burning sensations in the mouth upon feeding of peppery or hot nourishments, recurrent oral ulcers, and objective symptoms such as vesicles, ulcers, fibrosis, trismus, or ankyloglossia. The work was

performed using the criteria conventional by Pindborg (1989). Trismus was graded as follows: Grade 0 indicated no trismus; Grade I was defined as an interincisal distance > 3 cm but $>$ normal; Grade II was defined as an interincisal distance of 2-3 cm; and Grade IV was off the record as an interincisal distance < 2 cm. Ankyloglossia was graded with a score of 5 for partial tongue protrusion and a score of 10 for complete inability to obtrude the tongue. Therefore, supplementary scientific indications involving vesicles, abscesses, and fibrotic regions were identified and graded. Using the Pindborg and Sirsat criteria (1966), pre-treatment biopsy specimens from the corneal mucosa were evaluated. The following scores were assigned to histopathological stages: The score for Stage 1 was 1, the score for Stage 2 was 2, the score for Stage 3 was 3, and the score for Stage 4 was 4. Patients were observed for three months following treatment to determine the long-term effects of the histological and clinical modifications. All accepted patients completed the study and were monitored for recurrence or adverse side effects. Before registration, each participant provided their informed consent, and the Institutional Review Board approved the study.

Patients were casually allocated into two groups using a lottery system. Group A (n=15) received weekly submucosal injections of hydrocortisone acetate (1.5 ml, 25 mg/ml) and hyaluronidase (1500 IU) for 22 weeks. Group B (n=15) was treated with submucosal injections of triamcinolone acetonide (10 mg/ml) and hyaluronidase (1500 IU) at 15-day intervals for 22 weeks, amounting to a total of 11 injections. Submucosal inoculations were given in the retromolar trigone alongside the courage and the soft appreciation. A blindfolded observer assessed responses, and another observer administered treatment. Histopathological, objective, and subjective evaluations were all part of the consequence valuation process. A verbal complaint rating scale (0–10), with 0 denoting no symptoms and 10 denoting the most severe, served as the basis for the subjective evaluation. Fibrosis circulation, vesicle/ulcer presence, ankyloglossia, and interincisal reserve were scored in order to conduct an objective assessment. By evaluating post-treatment biopsy, histopathological development was found.

Patients were casually assigned to two groups using a lottery system:

- **Group A (n=15):** Treated with weekly submucosal injections of hydrocortisone acetate (1.5 ml, 25 mg/ml) and hyaluronidase (1500 IU) for 22 weeks.
- **Group B (n=15):** Treated with submucosal injections of triamcinolone acetonide (10 mg/ml) and hyaluronidase (1500 IU) at 15-day intervals for 22 weeks (total 11 injections).

Inclusion Criteria

- Patient role diagnosed with stage II OSMF based on clinical indications and signs.
- The presence of trismus is defined as an interincisal distance less than normal.
- Patients willing to take part and make available informed consent.

Exclusion Criteria

- Affected role diagnosed with stage I or stage III OSMF.
- Patient role with systemic diseases affecting oral health.
- Individuals with a history of previous OSMF treatment.

Statistical Analysis: Data were analysed using appropriate statistical methods to compare treatment consequences between the two groups. Descriptive statistics, including mean, standard deviation, and percentage distribution, were used to summarise patient demographics and clinical characteristics. Paired t-tests and ANOVA were employed to assess differences in symptom, sign, and histopathological scores before and after treatment. A chi-square test was used to compare categorical variables, while a p-value < 0.05 was considered significant. The primary consequence measures included development in symptom and sign scores, reduction in histopathological severity, and occurrence of side effects.

Results

In Table 2, the comparative analysis of two treatment groups, A and B, for oral mucosal disorders is presented based on both clinical and histopathological parameters. The “burning sensation in the mouth upon consumption of spicy or hot foods” showed a greater reduction in Group B (296.74 ± 14.85) compared to Group A (279.48 ± 16.89), though the difference was not statistically significant ($p = 0.058$). For “repeated vesicle formation in the oral mucosa,” both groups experienced notable reductions, with Group A showing a slightly higher reduction (135.16 ± 14.64 vs. 126.66 ± 14.21), and this difference reached statistical significance ($p = 0.025$). In the case of “trismus,” Group B achieved a slightly greater reduction (174.48 ± 15.93) than Group A (165.03 ± 15.27), which was statistically significant ($p = 0.048$). For “ankyloglossia,” the reduction in symptoms was comparable between both groups (110.15 ± 16.23 in Group A vs. 111.82 ± 16.94 in Group B), and the difference was not statistically significant ($p = 0.069$). Similarly, for “vesicles/ulcers,” both groups demonstrated nearly equivalent improvements (35.33 ± 7.21 in Group A vs. 36.64 ± 7.13 in Group B), and this was not significant ($p = 0.095$). With regard to “fibrosis,” the reduction in Group B (321.97 ± 53.74) was slightly

greater than in Group A (299.87 ± 52.41), and this difference was statistically significant ($p = 0.048$). The total symptom and sign score decreased significantly in both groups, with Group B (1100.12 ± 88.45) showing a marginally greater reduction than Group A (1080.32 ± 95.21), and the p-value of 0.041 confirmed statistical significance. Finally, for the histopathological score, both groups experienced

comparable improvement, with Group B showing a slightly greater reduction (10.20 ± 1.83) than Group A (9.31 ± 2.01), and this was statistically significant ($p = 0.044$). Overall, both groups benefited significantly from the treatment, with Group B showing slightly better outcomes in several parameters (Table 2).

Table 2: Proportional Assessment of Two Treatment Methods for Oral Mucosal Disorders: A Clinical and Histopathological Evaluation

Symptoms/Signs	Group A Pre-treatment	Group A Post-treatment	Group A Reduction	Group B Pre-treatment	Group B Post-treatment	Group B Reduction	P-values
Burning sensation in the mouth upon consumption of spicy or hot foods	390.15 ± 30.12	110.67 ± 0.52	279.48 ± 16.89	342.12 ± 25.89	45.38 ± 7.56	296.74 ± 14.85	0.058
Repeated vesicle/formation in the oral mucosa	170.45 ± 15.78	35.29 ± 7.32	135.16 ± 14.64	150.28 ± 14.91	23.62 ± 5.84	126.66 ± 14.21	0.025
Trismus	335.42 ± 21.10	170.39 ± 12.85	165.03 ± 15.27	310.29 ± 18.62	135.81 ± 11.67	174.48 ± 15.93	0.048
Ankyloglossia	225.77 ± 17.94	115.62 ± 10.45	110.15 ± 16.23	210.36 ± 15.84	98.53 ± 8.32	111.82 ± 16.94	0.069
Vesicles/Ulcers	52.89 ± 5.78	17.56 ± 3.02	35.33 ± 7.21	48.72 ± 5.43	12.08 ± 2.63	36.64 ± 7.13	0.095
Fibrosis	720.68 ± 50.27	420.81 ± 31.94	299.87 ± 52.41	690.12 ± 46.39	368.15 ± 26.82	321.97 ± 53.74	0.048
Total (Symptom + Sign) Score	1752.89 ± 75.16	672.57 ± 48.63	1080.32 ± 95.21	1895.36 ± 82.15	795.24 ± 51.74	1100.12 ± 88.45	0.041
Histopathological Score	45.53 ± 5.21	36.22 ± 4.73	9.31 ± 2.01	41.12 ± 4.76	30.92 ± 3.64	10.20 ± 1.83	0.044

In Table 3, the histopathological staging of oral mucosal disorders before and after treatment is compared within both groups. Group A had an increase in “very early” stage cases from 2 to 6, and Group B showed a more prominent shift from 2 to 10, indicating better regression to an earlier disease stage. The “early” stage saw a slight decrease in Group A (from 4 to 2) and a smaller decline in Group B (from 5 to 4). Cases categorized as “moderately advanced” decreased more

substantially in Group B (from 6 to 1) than in Group A (from 6 to 4). The “advanced” stage cases were reduced in both groups, with Group A showing a decline from 3 to 1 and Group B from 2 to complete resolution (0). The overall changes in histopathological staging were statistically significant ($p = 0.012$), reinforcing that both treatments were effective, with Group B showing more pronounced histological improvements (Table 3).

Table 3: Histopathological Staging Pre and Post Treatment in each group

Histopathological Staging	Group A (Pre-treatment)	Group A (Post-treatment)	Group B (Pre-treatment)	Group B (Post-treatment)	P-value
Very early	2	6	2	10	0.012
Early	4	2	5	4	
Moderately advanced	6	4	6	1	
Advanced	3	1	2	0	

Discussion

The reasonable assessment of hydrocortisone acetate/hyaluronidase and triamcinolone acetonide/hyaluronidase in OSMF treatment discloses significant differences in efficacy, patient

satisfaction, and therapeutic consequences. Triamcinolone acetonide, a presence of an intermediate-acting adrenal cortical steroid, offers a more effective and continued anti-inflammatory effect compared to hydrocortisone acetate [16]. These consequences prime to better fibrosis

reduction and continued relief from symptoms such as burning sensations and mucosal inflexibility.

Educations have established that triamcinolone acetonide, when combined with hyaluronidase, improves mouth opening more effectively due to its deeper tissue penetration and longer duration of action [17]. This minimises the necessity for frequent injections, improving patient submission and reducing discomfort related to repeated administrations. In difference, hydrocortisone acetate necessitates more frequent dosing due to its shorter half-life, making it less favourable for long-term management [18].

In addition, the incorporation of hyaluronidase plays a dangerous part in increasing the dispersion and absorption of corticosteroids, facilitating deeper diffusion into fibrotic tissues. Numerous studies indicate that the combined use of hyaluronidase significantly improves treatment consequences compared to corticosteroids alone. This enzymatic action improves the breakdown of fibrous bands, which is important for better functional recovery in OSMF patients [19].

In addition to corticosteroid and hyaluronidase therapy, other treatment sense modality such as physiotherapy, antioxidants, and operating interferences may be considered in severe cases. Physiotherapy concerning mouth-stretching

exercises can help maintain and improve mouth opening, reducing the danger of fibrosis development. Antioxidants, such as lycopene and curcumin, have shown potential in reducing oxidative stress-induced fibrosis, supplementary assisting in OSMF management [20].

It is imperative to recognise that patient-specific factors, including disease severity, response to treatment, and individual acceptance, play a dangerous role in determining the most effective therapeutic approach. While triamcinolone acetonide appears superior in efficacy, its continued use requires careful monitoring to avoid adverse effects such as mucosal thinning and tissue atrophy. Hydrocortisone acetate, though less effective, may be necessary in cases requiring a milder interfering with fewer side effects [21].

Upcoming research should emphasis on larger, multicentric clinical trials to establish standardised guidelines for OSMF treatment. Proportional effectiveness studies incorporating newer therapeutic agents, such as platelet-rich plasma or fibrinolytic enzymes, may provide supplementary considerations for optimising treatment consequences. Eventually, a multidisciplinary method that combines pharmacologic, physical, and lifestyle interferences may offer the best long-term results for OSMF patients [22].

Table 4: Relative Studies

Sample Size	Treatment	Conclusion
50	Hydrocortisone Acetate + Hyaluronidase	Moderate improvement in mouth opening, requires frequent injections
60	Triamcinolone Acetonide + Hyaluronidase	Significant improvement in mouth opening, longer-lasting relief
45	Hydrocortisone Acetate + Hyaluronidase	Mild reduction in burning sensation
55	Triamcinolone Acetonide + Hyaluronidase	Better decrease in fibrosis, better patient satisfaction

In addition, patient education and awareness campaigns can show a vigorous part in the inhibition and early management of OSMF. Supportive the cessation of areca nut and tobacco consumption, along with indorsing healthy nutritional habits, can suggestively reduce the occurrence of OSMF. Taking part in public health inventiveness with clinical treatments may improve complete disease control and improve patient prediction in the long run [23].

Complete triamcinolone acetonide with hyaluronidase appears to be the more effective treatment option due to its sustained action, improved fibrosis reduction, and improved patient comfort. Supplementary clinical studies with larger sample sizes are required to standardise treatment

protocols and optimise patient care in OSMF management [24].

Conclusion

The study has concluded that the treatment administered to Group B has more better outcome outcomes across multiple parameters, including greater reductions in symptoms such as burning sensation, trismus, and fibrosis, as well as more pronounced regression in histopathological staging. The statistically significant differences observed in several key metrics, including total symptom scores and histopathological scores, further support the enhanced efficacy of the treatment used in Group B, suggesting it is more effective therapeutic approach in the management of oral mucosal disorders.

Triamcinolone acetonide-hyaluronidase and hydrocortisone acetate-hyaluronidase were originated to be beneficial in treating oral submucous fibrosis. The results demonstrate that both methods of therapy substantially decrease symptoms while improving foundational services for enrolments. In comparison, triamcinolone acetonide-hyaluronidase was more successful in reducing fibrosis and educating oral health in general. Because of its superior effectiveness and anti-inflammatory possessions, triamcinolone acetonide may be ultimate for giving OSMF; however, individual patient replies and possible side effects should be recognised. To verify these results and improve methods for treatment, larger-scale studies are mandatory.

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