REVIEW ARTICLE AND CASE REPORT ON ORAL SUBMUCOUS FIBROSIS

Dr Abhay Goswami[1], Dr V Raj Kumar[2], Dr Kinjal Babel[3], Dr DEV HR[4], Nimbalkar Kajol Ranjit[5]

[1,3,5]Post Graduate 3rd Year; OMFS, Jaipur Dental College
[2]Professor and head, Dept. of OMFS, Jaipur Dental College
[4]Public Health Dentistry, Assistant Professor, BIDS; Bengaluru
Email: abhaygoswami847@gmail.com

ABSTRACT: Oral Submucous Fibrosis (OSMF) is a chronic, progressive, potentially malignant disorder predominantly associated with areca nut chewing. Histologically, It is characterized by juxta-epithelial inflammation, excessive collagen deposition, and fibrosis of the oral mucosa, resulting in progressive trismus and functional impairment. This review article represents various indepth features of combined intralesional therapy and anti oxidant therapy in osmf, based on the case report of a 46-year-old patient.

How to cite this article: Goswami A, Raj Kumar V, Babel K, Dev HR, Ranjit NK. Review Article and Case Report on Oral Submucous Fibrosis. Int J Drug Deliv Technol. 2026;16(69s): 1854-1862. DOI: 10.25258/ijddt.16.69s.184

INTRODUCTION

Oral Submucous Fibrosis (OSMF) is a chronic, progressive, potentially malignant disorder of the oral cavity characterized by juxta-epithelial inflammatory reactions and progressive fibrosis of the oral mucosa, leading to rigidity of oral tissues and restricted mouth opening. What begins as a seemingly harmless burning sensation when eating spicy food can quietly evolve over months and years into a rigid cage of fibrous tissue, severely locking the jaw—a debilitating clinical state known as trismus.[1,2]

The condition predominantly affects populations in South and Southeast Asia, particularly India, where the habit of areca nut chewing is highly prevalent. OSMF was first described by Schwartz in 1952 among Indian women residing in East Africa and later extensively studied by Pindborg and Sirsat in 1966.

OSMF is recognized as a significant public health problem due to its debilitating nature and its potential for malignant transformation into oral squamous cell carcinoma. The reported rate of malignant transformation ranges from 4% to 13%, making early diagnosis and effective management crucial. The etiology of OSMF is multifactorial, with areca nut chewing considered the principal causative factor. Other contributing factors include consumption of spicy foods, nutritional deficiencies, genetic predisposition, autoimmune mechanisms, and immunological alterations.

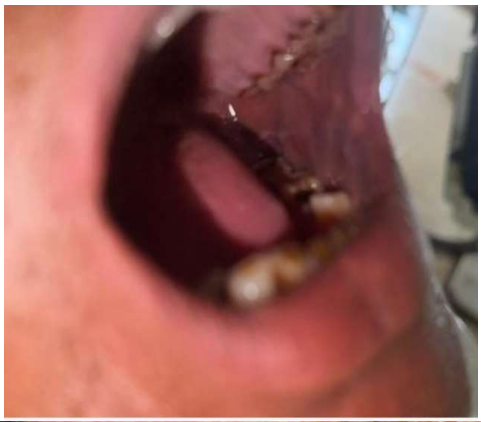
The pathogenesis of OSMF involves excessive collagen synthesis and reduced collagen degradation, resulting in accumulation of dense fibrous connective tissue within the oral mucosa. Alkaloids present in areca nut, particularly arecoline, stimulate fibroblast proliferation and collagen production. Simultaneously, increased activity of lysyl oxidase, a copper-dependent enzyme, promotes collagen cross-linking, thereby enhancing fibrosis. Chronic inflammation and oxidative stress further contribute to tissue injury and disease progression.

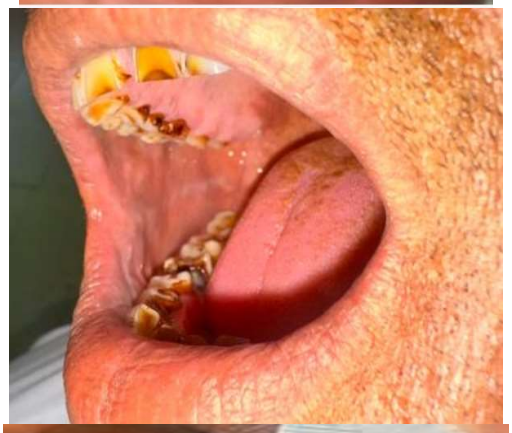
Clinically, patients with OSMF commonly present with burning sensation of the oral mucosa, intolerance to spicy foods, blanching and stiffness of oral tissues, reduced mouth opening (trismus), difficulty in speech and swallowing, and impaired oral hygiene maintenance. Histopathologically, the disease is characterized by epithelial atrophy, dense collagen deposition, hyalinization of connective tissue, and varying degrees of inflammatory cell infiltration.[1,3]

CASE-REPORT: -

A 46-year-old male patient visited OMRD department of Jaipur dental college and hospital with chief complain as reduced mouth opening along with burning sensation specially while having hot and spicy food, after following basic protocols of hospital, patient was referred to Department of oral and maxillofacial surgery.

On Examination:- There was a reduced mouth opening of 15mm on measuring with Vernier caliper for precise measurement , with the help of team , fibrous bands were palpated on the right and left buccal mucosa ,extending from retromolar area to commissure of lip and certain bands were observed in palatal area too.





ABOVE PICTURES REPRESENTING OSMF IN A PATIENT ALONG WITH THEIR MOUTH OPENING DURING THEIR FIRST VISIT

There was no relevant medical history given from patient

Adverse habits history: -Patient had a habit of tobacco chewing almost since a decade, consuming an average of 5-6 packets of tobacco per day ,as well as 2-3 cigarettes of smoking per day.

MANAGEMENT: -

Patient was given -intralesional injections by palpating the fibrous bands- Combined with local anaesthesia [to reduce pain] along with triamcinolone 40 mg and hyaluronic acid in first month twice weekly 2nd moth once weekly 3rd month once in 15 days

Orally, spirulina- 1 cap per day + omega 3 fatty acid 1 capsule per day till treatment is ongoing and **topically** wysolone 5 mg tablet [to be crushed] and use it as mouthwash once daily along with aloe-vera gel - twice daily.

Regular follow up was done for a patient, downline 3 months; mouth opening was increased by 21mm and patient was able to open mouth by nearly 36mm.

Patient was motivated and psychological counselling was also done for tobacco cessation in the Jaipur dental college and hospital

PICTURE SHOWING MOUTH OPENING POST-PHARMACOTHERAPY

ETIOLOGICAL FACTORS: -

Areca Nut

Areca nut (Areca catechu) is regarded as the principal etiological agent responsible for the development of OSMF. It is consumed in various forms including raw nut, roasted nut, boiled nut, betel quid, pan masala, and gutkha.

Pathogenesis

The pathogenic effects of areca nut are attributed to its alkaloids and polyphenols.

These alkaloids stimulate fibroblast proliferation and enhance collagen synthesis while simultaneously inhibiting collagen degradation. As a result, excessive collagen accumulates within the submucosal tissues leading to fibrosis.

Areca nut also contains high concentrations of tannins and catechins that stabilize collagen fibers, making them resistant to enzymatic degradation.

In addition, copper present in areca nut activates lysyl oxidase, an enzyme responsible for collagen cross-linking, thereby increasing fibrosis.[4,5]

2. Tobacco [Same habit was observed in present case-report patient]

Although tobacco alone rarely causes OSMF, it significantly aggravates disease progression when consumed with areca nut.

Role in OSMF

Tobacco contributes through:

- Increased oxidative stress
- DNA damage
- Chronic mucosal irritation
- Reduced vascularity
- Increased inflammatory cytokines
- Enhanced epithelial dysplasia

Nicotine and tobacco-specific nitrosamines induce epithelial alterations that increase the malignant transformation potential of OSMF.

Patients who consume both areca nut and tobacco exhibit:

- Earlier onset
- Greater fibrosis
- Higher incidence of epithelial dysplasia
- Increased oral cancer risk

3. Gutkha

Gutkha is a commercially manufactured preparation containing:

- Areca nut
- Tobacco
- Slaked lime
- Catechu
- Flavoring agents
- Sweeteners

It has become one of the strongest risk factors for OSMF because it delivers concentrated areca nut and tobacco directly to the oral mucosa.

Several studies report that habitual gutkha users have a substantially higher risk of developing OSMF compared with users of conventional betel quid.[6-8]

4. Pan Masala

Pan masala is a commercially available mixture containing:

- Areca nut
- Catechu
- Cardamom
- Flavoring agents
- Sweeteners
- Lime

Although some formulations do not contain tobacco, they remain highly fibrogenic because of their high areca nut content.

Easy availability, attractive packaging, and aggressive marketing have contributed significantly to increased consumption among school-aged children and adolescents.

5. Commercial Preparations

Commercial preparations have become the leading contributors to the rising prevalence of OSMF.

These products include:

- Gutkha
- Pan masala
- Supari
- Sweet supari
- Flavored areca nut
- Tobacco sachets
- Flavored chewing mixtures

Nutritional Deficiencies

Deficiencies of:

- Iron
- Vitamin B complex
- Vitamin A
- Vitamin C

may impair mucosal repair and increase vulnerability to fibrosis.

Immunological Factors

Elevated levels of inflammatory mediators have been reported, including:

- TNF-α
- IL-6
- TGF-β

These cytokines stimulate fibroblast activation and collagen deposition.[9-11]

Chronic Mechanical Irritation

Repeated trauma from:

- Sharp teeth
- Ill-fitting dentures
- Continuous chewing

Environmental Factors

Exposure to:

- Capsaicin-rich spicy foods
- Nutritional imbalance
- Poor oral hygiene

may contribute as secondary risk factors.[12,13]

BEHAVIOURAL MANAGEMENT

Recognizing the addictive nature of smokeless tobacco is crucial for understanding the challenges of quitting. Tobacco usage in all its forms has been identified as the primary cause of cancer. Nicotine, highly addictive and present in products like chewing tobacco and snuff, leads to physical and psychological dependence.

Smokeless tobacco, integrated into daily routines, is strongly linked to various cancers and oral health issues such as gum disease and tooth decay. The abrasive nature of these products can cause irritation, leading to white patches or lesions in the mouth. Some people may not completely comprehend the health concerns connected with the use of smokeless tobacco, or they may underestimate the difficulties of quitting. It is critical to raise awareness about the harmful effects of smokeless tobacco and provide education on quitting possibilities.

Social Cognitive Theory (SCT) is crucial in tobacco cessation counseling, highlighting the influence of observational learning, self-efficacy, and environmental factors on behavior change. [14]

In smoking cessation, counselors utilize **SCT principles** to offer role models who have successfully quit, boosting individuals' confidence in their ability to quit. Counselors address cognitive restructuring to help clients challenge and modify beliefs associated with smoking. SCT offers a holistic framework, customizing interventions to the cognitive, social, and environmental aspects of individuals' tobacco cessation journeys. This contributes to a more comprehensive and effective counseling approach.

The Health Belief Model (HBM) guides tobacco cessation counseling by emphasizing individuals' perceptions of health risks linked to smoking and their beliefs in quitting efficacy. This counseling approach assesses perceived susceptibility to smoking-related health issues, severity of consequences, and perceived benefits and barriers to quitting. The Health Belief Model offers a framework to understand and address cognitive and perceptual factors in an individual's decision-making about tobacco use. This enhances the effectiveness of tobacco cessation counselling.

The Transtheoretical Model (TTM) is a stage-based theory of behavior changes. The stages are pre-contemplation (not intending to change soon), contemplation (change is being considered but not definitely planned), preparation (behavior change is imminent), action (behavior change is occurring), and maintenance (behavior change has been consolidated).[15-17]

REVIEW

Based on articles from indexed journal , Various treatment modalities have been employed for the management of OSMF, including habit cessation, nutritional supplementation, physiotherapy, intralesional injections, antioxidants, and surgical intervention in advanced cases.

Among these, intralesional therapy has gained considerable attention because it delivers therapeutic agents directly into the fibrotic tissue, producing higher local concentrations with minimal systemic effects. Intralesional corticosteroids such as dexamethasone and triamcinolone acetonide reduce inflammation and fibroblast activity, while hyaluronidase facilitates degradation of the extracellular matrix and improves tissue elasticity. Combination intralesional therapy has been reported to provide better symptomatic relief and improvement in mouth opening compared to monotherapy.

Oxidative stress has emerged as a key factor in the pathogenesis of OSMF. Reactive oxygen species generated during areca nut chewing cause cellular damage, lipid peroxidation, and activation of fibrogenic pathways. Consequently, antioxidant therapy has been widely incorporated into OSMF management protocols. Antioxidants such as lycopene, beta-carotene, vitamins A, C, and E, and spirulina help neutralize free radicals, reduce oxidative stress, improve mucosal health, and enhance tissue healing.[18-20]

Recent studies suggest that combining intralesional therapy with antioxidant supplementation may offer synergistic benefits in OSMF management. While intralesional agents directly target fibrosis and inflammation, antioxidants address the underlying oxidative damage and improve the overall tissue environment. This combined therapeutic approach may result in greater improvement in mouth opening, reduction in burning sensation, enhanced quality of life, and potentially reduced disease progression.

Despite the availability of multiple treatment modalities, there remains no universally accepted standard treatment protocol for OSMF. Therefore, evaluating the efficacy of combined intralesional therapy and antioxidant therapy is important to establish evidence-based treatment strategies for improving clinical outcomes in patients with OSMF. The present study aims to assess the role and effectiveness of combined intralesional therapy and antioxidant therapy in the management of Oral Submucous Fibrosis.[21-24]

JUSTIFICATION FROM VARIOUS ARTICLES STATING OSMF IS MORE DESTRUCTIVE AS COMPARED TO OTHER CANCEROUS LESION:-

The underlying biological mechanisms explain why this habit is so destructive:

- **Alkaloid Activation:** Areca nuts contain specific alkaloids—chiefly **arecoline**—that overstimulate fibroblasts, the specialized cells responsible for producing structural proteins in our tissues.
- **Collagen Overproduction:** This constant stimulation triggers an aggressive overproduction of collagen.
- **Tissue Hardening:** Simultaneously, the chemical compounds block the body's natural mechanisms for breaking down excess protein. This net imbalance locks the oral mucosa into a cycle of dense, inflexible scarring [25,26]

Recognizing the Early Warning Signs

Because the onset of OSMF is highly gradual, early clinical indicators are frequently ignored or misdiagnosed as routine mouth ulcers. In its initial phases, patients typically report:

- A persistent, localized burning sensation (stomatopyrosis), heavily exacerbated by spicy, salty, or acidic foods.
- Blistering, recurrent ulcers, and a noticeable drying of the mouth due to reduced salivary flow.
- A distinct blanching of the oral mucosa, where the healthy, vibrant pink tissues of the inner cheeks, soft palate, and gums fade into a marbled, chalky-white appearance.

As the condition advances, dense, palpable fibrous bands form vertically along the inner cheeks. These bands act like tightening cords, drastically reducing the mouth's flexibility and restricting the movement of the tongue.[27]

At its core, Oral Submucous Fibrosis is a disease of unregulated tissue repair. The delicate oral mucosa transitions from a soft, elastic membrane into a dense, scarred matrix because the biological "cruise control" for collagen production breaks down. To understand how this happens, we must look at the specific cellular and molecular changes triggered by the components of the areca nut.

The Collagen Imbalance Equation

Under healthy conditions, fibroblasts (the primary structural cells of connective tissue) maintain a strict balance between producing collagen for tissue strength and secreting enzymes called **Matrix Metalloproteinases (MMPs)** to break down old collagen. In OSMF, this equation is heavily disrupted in two distinct phases:

1. Hyper-Activation of Collagen Production

Areca nut alkaloids—specifically **arecoline, arecaidine, guvacoline, and guvacine**—penetrate the oral lining and stimulate fibroblasts to work overtime. Arecoline upregulates **TGF-β (Transforming Growth Factor-beta)**, a powerful signaling protein that functions as the body's primary pro-fibrotic switch.

When TGF-β is over-activated, it forces fibroblasts to differentiate into **myofibroblasts**. These specialized cells possess contractile properties (similar to smooth muscle cells) and pump out massive amounts of Type I and Type III collagen directly into the submucous layer of the mouth.

2. Shutdown of Collagen Degradation

The body has a built-in defense mechanism to dissolve excess collagen using MMPs. However, arecoline simultaneously stimulates fibroblasts to overproduce **TIMPs (Tissue Inhibitors of Metalloproteinases)**.

Think of TIMPs as chemical handcuffs that bind to and deactivate MMPs. With the degradation machinery turned off, the newly formed, dense collagen fibers cannot be broken down. They pile up continuously, cross-linking with one another to form rigid, immovable structures.

Copper as a Catalyst

The areca nut also introduces high concentrations of soluble **copper**. This trace element acts as an essential cofactor for **lysol oxidase (LOX)**, an enzyme responsible for cross-linking collagen fibers.

The spike in local copper levels supercharges LOX activity, cross-linking the excess collagen into highly stable, insoluble bundles that resist any natural attempts at cellular cleanup.

The Ischemia-Malignancy Connection: As the dense collagen fibers tightly pack together, they crush the surrounding micro-vessels. This creates a state of severe local **ischemia** (lack of blood supply) and **hypoxia** (oxygen deprivation). Deprived of oxygen, the thinned oral epithelium is forced to undergo cellular mutations, explaining why advanced OSMF has a malignant transformation rate hovering between **7% to 13%**.

Conservative Management of Oral Submucous Fibrosis

When treating Oral Submucous Fibrosis, the primary goals are to alleviate symptoms (like the persistent burning sensation), arrest the progression of tissue scarring, and improve jaw mobility.

For patients presenting in the **early to moderate clinical stages (Stages I and II)**—where the fibrous bands have not yet locked the jaw completely—**conservative management** is the gold standard. This non-surgical approach relies on a combination of behavioral modifications, local and systemic medical therapies, nutritional support, and physical therapy.

1. Absolute Cessation of Habit (The Non-Negotiable Step)

No medical intervention will succeed if the underlying trigger remains active. The absolute first step in conservative management is the complete termination of areca nut, tobacco, gutkha, pan masala, and alcohol consumption.

Clinical Reality: Continued chewing of areca nut continuously pumps arecoline and copper into the tissues, overstimulating myofibroblasts and completely neutralizing the effects of therapeutic drugs. Behavioral counseling and support systems are essential to help the patient break the habit permanently.

2. Pharmacological Interventions

Medical management aims to break down existing collagen, reduce local inflammation, and restore blood flow to the oxygen-starved oral tissues. This is typically achieved through a combination of local injections and oral medications.

Intralesional Injection Therapy

For localized, dense fibrous bands, clinicians deliver medications directly into the submucous layer via weekly or bi-weekly injections. This local delivery

bypasses systemic side effects and concentrates the therapeutic agents exactly where they are needed.[2,28,29]

- **Corticosteroids (e.g., Triamcinolone Acetonide 10-40 mg/mL):** These powerful anti-inflammatory agents work by inhibiting the pro-fibrotic signaling protein TGF-β. By suppressing the inflammatory response, they reduce fibroblast proliferation and decrease the burning sensation.
- **Proteolytic Enzymes (e.g., Hyaluronidase 1500 IU):** Often mixed directly with the steroid injection, hyaluronidase breaks down hyaluronic acid—a core component of the tissue matrix. This lowers the viscosity of the connective tissue, breaks down early collagen cross-links, and allows the steroid to distribute more effectively.
- **Placental Extract (e.g., Placentrex):** Derived from human term placenta, this extract acts as a local biogenic stimulator. It possesses powerful anti-inflammatory properties, stimulates local blood vessel growth (neovascularization), and helps reverse the tissue ischemia (blood starvation) caused by dense scarring.

Systemic (Oral) Medications

To complement local injections, oral medications are prescribed to improve peripheral blood circulation and combat cellular stress.

- **Pentoxifylline (400 mg, 2-3 times daily):** A methylxanthine derivative that acts as a peripheral vasodilator. It improves microcirculation by increasing red blood cell flexibility, reducing blood viscosity, and inhibiting fibroblast activity. This brings essential oxygen back to the hypoxic (oxygen-deprived) tissues.
- **Lycopene (16-20 mg daily):** A powerful antioxidant extracted from tomatoes. Lycopene neutralizes free radicals, inhibits the growth of abnormal cells, and downregulates collagen production, making it highly effective at lowering the risk of malignant transformation.

3. Nutritional and Antioxidant Therapy

Because a thinned out (atrophic) oral mucosa is highly susceptible to dietary deficiencies, replenishing the body's micronutrient stores is crucial for tissue repair.

- **Iron and Vitamin B-Complex Supplementation:** Chronic iron deficiency anemia leads to a decrease in cytochrome oxidase enzymes, which further compromises the oral epithelium. Restoring iron and B-complex levels helps rebuild the mucosal barrier.
- **Vitamins A, C, and E:** These synergistic antioxidants protect epithelial cell membranes from oxidative damage and assist in normal, healthy tissue remodeling.[26,30]

4. Physical Therapy: Physiotherapeutic Exercises

Medical therapy can soften tissue, but **physical movement** is what actually stretches the fibrous bands and restores the interincisal opening. Physical therapy must be practiced consistently by the patient at home, 4 to 5 times a day.

- **Forceful Mouth Opening Exercises:** Patients are taught to use mechanical aids like an **acrylic cone**, **side-pinching mouth gags**, or a stack of **wooden tongue blades (spatulas)**. By gradually adding one more tongue blade to the stack over time, the patient applies a constant, gentle stretch to the rigid bands.
- **Voluntary Exercises:** Simple movements like wide yawning, blowing air into the cheeks, and moving the tongue in a circular motion help maintain mucosal elasticity and prevent further relapse.[10-16]

DISCUSSION

Considering the case report , The patient was prescribed oral spirulina supplementation throughout the treatment period as Spirulina possesses potent antioxidant, anti-inflammatory, and immunomodulatory properties owing to its **high content of β-carotene**, phycocyanin, vitamins, and essential amino acids. Previous studies have demonstrated that spirulina supplementation can significantly improve burning sensation and mouth opening in patients with OSMF by reducing oxidative stress associated with the disease.

The rationale for combining intralesional therapy with antioxidant supplementation lies in their complementary mechanisms of action. While corticosteroids and hyaluronidase act directly on the fibrotic tissue, antioxidants target the oxidative stress and inflammatory pathways that contribute to disease progression. This multimodal approach is expected to provide both symptomatic relief and disease modification.[17]

One of the earliest studies evaluating combined therapy was conducted by Niranzena Panneer Selvam and Arjun Anand Dayanand. Their study compared oral lycopene with intralesional steroids and hyaluronidase, antioxidant capsules with intralesional therapy, and intralesional therapy alone. The authors reported significantly greater improvement in mouth opening and reduction in burning sensation in the groups receiving antioxidants in addition to intralesional injections compared with intralesional therapy alone. The lycopene-containing regimen showed the most favorable outcomes, suggesting a

synergistic effect between antioxidant supplementation and intralesional agents.[31,32]

Evidence from systematic reviews and network meta-analyses further strengthens the concept of combined therapy. A network meta-analysis comparing multiple interventions for OSMF ranked the combination of lycopene, corticosteroids, and hyaluronidase among the most effective regimens for improving mouth opening. The authors suggested that therapies targeting both fibrosis and oxidative stress may achieve superior clinical outcomes compared with monotherapies.[33]

Aloe vera is a mannoprotein containing many amino acids known as 'wound healing hormones'. Aloe vera has been used for a very wide range of conditions. The polysaccharides contained in the gel of the leaves, promote wound healing, and have anti-inflammatory, immunomodulatory, antioxidant properties and gastro protective properties. Further, sterols in the Aloe vera have strong ability to inhibit inflammation similar to the action of cortisone without any side effects. It can be found easily and is of low cost in India.[34]

It has been said that topical application of the aloe vera gel can be used as a preventive or treatment modality for radiation induced skin reactions.

Spirulina is a microalga with rich natural source of pro teins, carotenoids and other micronutrients and used in daily diet of African and American natives. It contains phenolic acid, tocopherols, and betacarotene which are known to exhibit antioxidant properties.9 Spirulina has been used for the treatment of several oral mucosal lesions with successful results. It has been primarily assessed in treating leukoplakia with promising results.[21,13]

Prednisolone Inhibits phospholipase A_2, reducing prostaglandin and leukotriene synthesis, Suppresses migration of inflammatory cells,Decreases capillary permeability and tissue edema, Reduces cytokine production and immune responses.[26,27,35-37]

Similar results were observed in the current case report and the points provided by , **Singh et al** have shown significant improvement in mouth opening, hyperkeratosis, pain in mouth and size of the lesion with oxitard capsules.

Rajendran et al found significant results with mouth opening and burning sensation with pentoxifylline, although results with tongue protrusion were not significant. Lycopene has also showed significant improvement in mouth opening in the study **by Karemore et al.**

Sudarshan et al have shown significant improvement in the mouth opening with aloe vera.[38-40]

FUTURE PERSPECTIVE AND PUBLIC HEALTH SIGNIFIANCE:-

Despite significant progress in understanding and managing oral submucous fibrosis (OSMF), several challenges remain that warrant further investigation. Future research should focus on elucidating the molecular and genetic mechanisms underlying disease initiation, progression, and malignant transformation. A deeper understanding of the pathogenic pathways may facilitate the identification of novel therapeutic targets and predictive biomarkers for early diagnosis and disease monitoring.

Advances in regenerative medicine, including stem cell therapy, tissue engineering, and growth factor-based approaches, offer promising opportunities for restoring normal oral mucosal architecture and function. In addition, targeted drug delivery systems such as nanoparticles, liposomes, and biodegradable scaffolds may improve the bioavailability and therapeutic efficacy of antifibrotic agents while minimizing systemic adverse effects.

Mesenchymal stem cells (MSCs), particularly those derived from bone marrow and adipose tissue, possess anti-inflammatory, antifibrotic, immunomodulatory, and angiogenic properties that may help reverse fibrosis, promote tissue regeneration, and improve mouth opening.

The development of standardized treatment protocols through multicenter, randomized controlled clinical trials with larger sample sizes is essential to establish evidence-based guidelines for OSMF management. Future studies should also evaluate long-term treatment outcomes, recurrence rates, quality of life, and the prevention of malignant transformation.

Stem cell therapy has emerged as a promising regenerative strategy for the management of oral submucous fibrosis (OSMF).

Combination therapy integrating pharmacological agents, physiotherapy, nutritional supplementation, and minimally invasive surgical techniques is likely to remain a promising treatment strategy. Furthermore, advances in artificial intelligence and digital health technologies may facilitate early screening, risk stratification, and personalized treatment planning.

Public health initiatives emphasizing tobacco and areca nut cessation, community awareness, and routine oral cancer screening should be strengthened to reduce the incidence and disease burden of OSMF. Collaborative research involving clinicians, oral pathologists, molecular biologists, and biomedical engineers will be instrumental in developing innovative, patient-centered therapeutic approaches. Ultimately, translating emerging scientific discoveries into clinical practice will improve treatment outcomes and reduce the risk of malignant transformation associated with OSMF.

CONCLUSION: -

Combined intralesional therapy and antioxidant therapy represent a promising, safe, and effective conservative management strategy for Oral Submucous Fibrosis.

By addressing both fibrosis and oxidative stress, this therapeutic combination offers better clinical outcomes and may contribute significantly to improving the prognosis and quality of life of affected individuals. Continued research is warranted to optimize treatment protocols and strengthen the evidence base for routine clinical practice.

Based on case report, strict cessation of deleterious habits, patient compliance, and a multimodal conservative treatment approach can effectively reduce fibrosis, improve mouth opening, and enhance the quality of life in patients with OSMF. Long-term follow-up remains essential because OSMF is a potentially malignant disorder with a persistent risk of malignant transformation.

References

1. Schwartz J. Atrophia idiopathica (tropica) mucosae oris. Demonstrated at the 11th International Dental Congress; 1952; London, UK.
2. Singh M, Niranjan HS, Mehrotra R, Sharma D, Gupta SC. Efficacy of hydrocortisone acetate/hyaluronidase versus triamcinolone acetonide/hyaluronidase in the treatment of oral submucous fibrosis. **Indian J Med Res.** 2010;131(5):665-669.
3. Pindborg JJ, Sirsat SM. Oral submucous fibrosis. **Oral Surg Oral Med Oral Pathol.** 1966;22(6):764-779.
4. Warnakulasuriya S, Kujan O, Aguirre-Urizar JM, et al. Oral potentially malignant disorders: a consensus report from an international seminar. **Oral Dis.** 2021;27(8):1862-1880.
5. Arakeri G, Brennan PA. Oral submucous fibrosis: an overview of the aetiology, pathogenesis, classification, and principles of management. **Br J Oral Maxillofac Surg.** 2013;51(7):587-593.
6. Tilakaratne WM, Klinikowski MF, Saku T, Peters TJ, Warnakulasuriya S. Oral submucous fibrosis: review on aetiology and pathogenesis. **Oral Oncol.** 2006;42(6):561-568.
7. Angadi PV, Rao SS. Areca nut in pathogenesis of oral submucous fibrosis: revisited. **Oral Maxillofac Surg.** 2011;15(1):1-9.
8. Rajendran R. Oral submucous fibrosis: etiology, pathogenesis, and future research. **Bull World Health Organ.** 1994;72(6):985-996.
9. Kerr AR, Warnakulasuriya S, Mighell AJ, et al. A systematic review of medical interventions for oral submucous fibrosis and future research opportunities. **Oral Dis.** 2011;17(Suppl 1):42-57.
10. Gupta PC, Ray CS. Epidemiology of betel quid usage. **Ann Acad Med Singapore.** 2004;33(Suppl):31-36.
11. International Agency for Research on Cancer. **Betel-quid and areca-nut chewing and some areca-nut-derived nitrosamines.** IARC Monographs on the Evaluation of Carcinogenic Risks to Humans. Vol. 85. Lyon: IARC; 2004.
12. Babu S, Bhat RV, Kumar PU, et al. A comparative clinicopathological study of oral submucous fibrosis in habitual chewers of pan masala and betel quid. **Clin Toxicol.** 1996;34(3):317-322.
13. Hazare VK, Goel RR, Gupta PC. Oral submucous fibrosis, areca nut and pan masala use: a case-control study. **Natl Med J India.** 1998;11(6):299-301.
14. Vats S, Gupta R, Rajeev A, Gupta B, Sharma D, Mehrotra K. Behavioral modification strategies for tobacco cessation: a scoping review. **J Educ Health Promot.** 2024;13:419.
15. Bektas M, Ozturk C, Armstrong M. An approach to children's smoking behaviors using social cognitive learning theory. **Asian Pac J Cancer Prev.** 2010;11:1143-1149.
16. Topa G, Moriano JA. Theory of planned behavior and smoking: meta-analysis and structural equation model. **Subst Abuse Rehabil.** 2010;1:23-33.
17. Aveyard P, Massey L, Parsons A, Manaseki S, Griffin C. The effect of transtheoretical model-based interventions on smoking cessation. **Soc Sci Med.** 2009;68:397-403.
18. Warnakulasuriya S. Oral submucous fibrosis: a review. **J Oral Pathol Med.** 2007;36(10):575-580.
19. Khan S, Chatra L, Prashanth SK, Veena KM, Rao PK. Pathogenesis of oral submucous fibrosis. J Cancer Res Ther. 2012 Apr-Jun;8(2):199-203. doi: 10.4103/0973-1482.98970. PMID: 22842361.
20. Canniff JP, Harvey W. The aetiology of oral submucous fibrosis: the stimulation of collagen synthesis by extracts of areca nut.

Int J Oral Surg. 1981;10(Suppl 1):163-7. PMID: 6807873.

21. Kerr AR, Warnakulasuriya S, Mighell AJ, et al. Oral submucous fibrosis: a review of current management. **Oral Dis.** 2011;17(Suppl 1):34-39.
22. Rai A, Kaur M, Gombra V, Hasan S, Kumar N. Comparative evaluation of curcumin and antioxidants in the management of oral submucous fibrosis. J Invest Clin Dent. 2019;10(4):e12464.
23. Datarkar A, Akare A, Tayal S. Efficacy of Prednisolone Mouthwash in Management of Grade III oral Submucous fibrosis: a newer drug Regimen. J Oral Maxillofac Surg. 2020;19(4):532–8.
24. Mehrotra R, Singh HP, Gupta SC, Singh M, Jain S. Pentoxifylline therapy in the management of oral submucous fibrosis. Asian Pac J cancer Prevention: APJCP. 2011;12(4):971–4.
25. World Health Organization. **Oral potentially malignant disorders and oral cancer prevention guidelines.** Geneva: World Health Organization. *;2020*
26. Patel TL, Singh S. Comparative evaluation of treatment of oral submucous fibrosis with intralesional injections of dexamethasone and hyaluronidase versus triamcinolone acetonide and hyaluronidase. **J Evol Med Dent Sci.** 2015;4(81):14161-14166.
27. Almasri MA, Venugopal K, Keshini MP, Diwaker M, Das A, Yadav VK, Bhattacharya S. Comparing the efficacy of intralesional triamcinolone acetonide and hyaluronidase with placental extract in oral submucous fibrosis cases: original research. **Int J Health Sci.** 2022;(II):278-284.
28. Ek J, John B, Sharma A, Poorna TA, Pangarikar A, Raj V. Comparison of intralesional placentrex versus hyaluronidase and dexamethasone injection in the symptomatic management of stage II oral submucous fibrosis: a prospective study. **Indian J Otolaryngol Head Neck Surg.** 2023;75(4):3530-3534.
29. Goldar GK, Singh HP, Maurya MK, Kumar S, Chandra M, Singh AB, Verma V, Mishra A. A clinicopathological study of oral submucous fibrosis to evaluate the response after treatment with intralesional steroid versus intralesional steroid plus hyaluronidase. **Indian J Otolaryngol Head Neck Surg.** 2023;75(4):3057-3062.
30. Guo J, Xie H, Mao S, Liang M, Wu H. Efficacy of hyaluronidase combined with corticosteroids in treatment of oral submucous fibrosis: a meta-analysis of randomized controlled clinical trials. **J Oral Pathol Med.** 2020;49(4):311-319. doi:10.1111/jop.13009.
31. Selvam NP, Dayanand AA. Lycopene in the management of oral submucous fibrosis. **Asian J Pharm Clin Res.** ;2013.
32. Johny J, Bhagvandas SC, Mohan SP. Comparison of efficacy of lycopene and lycopene-hyaluronidase combination in the treatment of oral submucous fibrosis. **J Pharm Bioallied Sci.;** 2019.
33. Chen, X., Xie, H. & Guo, J. Drug treatment for oral submucous fibrosis: an update. *BMC Oral Health* **23**, 748 (2023). https://doi.org/10.1186/s12903-023-03488-9
34. Vedeswari CP, Jayachandran S, Ganesan S. In vivo autofluorescence characteristics of pre- and post-treated oral submucous fibrosis: a pilot study. Indian J Dent Research: Official Publication Indian Soc Dent Res. 2009;20(3):261–7.
35. Patil S, Al-Zarea BK, Maheshwari S, Sahu R. Comparative evaluation of natural antioxidants spirulina and aloe vera for the treatment of oral submucous fibrosis. **J Oral Biol Craniofac Res.** 2015;5(1):11-15.
36. Glick M, Greenberg MS, Lockhart PB, Challacombe SJ, editors. **Burket's Oral Medicine.** 13th ed. St. Louis: Elsevier; 2021.
37. Raizada MK, Sable DM. Clinical Assessment of Efficacy of Omega 3 in oral Submucous Fibrosis Patients - A Randomized Controlled Trial. Asian Pac J cancer Prevention: APJCP. 2022;23(4):1185–92.
38. Rajendran R, Rani V, Shaikh S. Pentoxifylline therapy: a new adjunct in the treatment of oral submucous fibrosis. **Indian J Dent Res.** 2006;17:190-198.
39. Karemore TV, Motwani M. Evaluation of the effect of newer antioxidant lycopene in the treatment of oral submucous fibrosis. **Indian J Dent Res.** 2012;23:524-528.
40. Sudarshan R, Annigeri RG, Sree Vijayabala G. Aloe vera in the treatment of oral submucous fibrosis: a preliminary study. **J Oral Pathol Med.** 2012; 41:755-761.