

Narrative Review

Oral Submucous Fibrosis: A Review on Different Treatment Modalities

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ABSTRACT

Background: Oral Submucous Fibrosis (OSMF) is a chronic, debilitating condition affecting the oral mucosa, leading to significant functional impairment. It is primarily induced by the chronic use of areca nut and its commercial products. The disease is characterized by juxta-epithelial inflammation and progressive fibrosis of the submucosal tissues, resulting in severe trismus, pain, and burning sensation in the mouth.

Objective: This review aims to systematically assess and synthesize the available literature on the various treatment modalities for OSMF, evaluate their effectiveness, and identify areas requiring further research.

Methods: A comprehensive search was conducted across multiple databases including PubMed, Scopus, Web of Science, and Google Scholar using keywords such as "Oral Submucous Fibrosis," "OSMF treatment," and "fibrosis management." Studies published in English without any restriction on publication date were included. The review process involved screening titles and abstracts, followed by a full-text review. The quality and relevance of studies were assessed, focusing on study design, sample size, methodological rigor, and impact on clinical practice. Quantitative data were extracted and synthesized where available.

Results: The search yielded a total of 150 studies, of which 45 met the inclusion criteria and were analyzed. Treatment modalities varied widely, including pharmacological interventions (corticosteroids, hyaluronidase, placental extracts), physical therapies (EZbite, acrylic splints, hyperbaric oxygen therapy), surgical techniques (fibrotomy, various flap reconstructions), and emerging therapies (stem cell treatment, omega-3 supplementation). Surgical interventions showed a success rate of 60-70% in improving mouth opening, while pharmacological treatments reported a 50-60% reduction in symptoms such as burning sensation and pain. The use of stem cells and omega-3 showed promising preliminary results but lacked extensive clinical trials.

Conclusion: The treatment of OSMF requires a multidisciplinary approach, combining pharmacological, physical, and surgical modalities. While current treatments show varying degrees of effectiveness, there is a need for more randomized controlled trials to establish the efficacy of emerging therapies. Future research should focus on developing less invasive and more targeted treatments to improve patient outcomes.

Keywords: Oral Submucous Fibrosis, OSMF treatment, fibrosis management, surgical intervention, pharmacological therapy, physical therapy, stem cell treatment, omega-3.

INTRODUCTION

Oral Submucous Fibrosis (OSMF) is a debilitating, progressive, and irreversible metabolic disorder of the collagen in the oral mucosa, often extending to the pharynx and esophagus. This condition is induced by chronic chewing of areca nut and its commercial preparations, leading to juxta-epithelial inflammation, fibrosis, and resulting in mucosal stiffness and functional morbidity (1-4). First identified by Schwartz in 1952 as "Atropica idiopathica mucosae oris," this condition was initially observed among five Indian women. The global distribution of OSMF reveals that over 2.5 million people are affected, predominantly in South and Southeast Asia (5-6). In India, the prevalence of OSMF varies between 0.2 to 2.3% in men and 1.2-4.6% in women, across a broad age spectrum of 11 to 60 years. The increasing incidence of OSMF, especially among the youth, is attributed to the commercialization of gutka and

flavoured supari, their widespread availability, and the influence of peer groups. The migration of populations has also led to a notable prevalence of OSMF in countries like South Africa, the United States, and Europe, thus expanding its global impact (7).

The rise in OSMF cases and the associated morbidity necessitates a comprehensive review of the effectiveness of current and newly developed treatment modalities. This review aims to summarize existing therapeutic strategies, incorporate recent clinical research, and foster discussion about potential treatment options. Key predisposing factors for OSMF include the chewing of areca nuts, in forms such as gutka or flavored supari, with studies from Pakistan, India, and Nepal indicating a malignant transformation rate of 7-30% (5). Other contributing factors include long-term consumption of betel leaf, areca nut, and lime, as well as nutritional deficiencies like Iron, vitamin B complex, and other minerals, leading to impaired healing of the oral mucosa and subsequent abnormal scarring and fibrosis (8).

Clinically, OSMF is diagnosed based on its stage and severity, initially presenting as a change in the color of the oral mucosa, a burning sensation after consuming spicy food, trismus, and eventually progressing to dysphagia, vesicle development, ulceration, recurrent stomatitis, hypersalivation, or xerostomia (9). In advanced stages, deafness has been reported (10). The absence of a well-established treatment plan poses significant challenges in managing OSMF. The primary treatment objectives are to alleviate symptoms, halt disease progression, and reduce the risk of malignant transformation (11). Treatment options include dietary supplements (vitamins and antioxidants), anti-inflammatory drugs (corticosteroids), proteolytic drugs (hyaluronidase and placental extracts), vasodilators, immunomodulators, and anti-cytokines.

Patients with OSMF commonly seek medical attention for symptoms like a burning sensation when eating spicy foods, difficulty in chewing and swallowing, and a progressive decrease in mouth opening. Enhancing mouth opening, either through medicinal or surgical means, is therefore a key focus in the management of OSMF. The choice between nonsurgical and surgical treatment depends on the clinical staging of the disease. Conventional treatments involve education and counseling to encourage patients to cease habits such as chewing betel nuts and areca nuts, particularly in the early stages of the disease, to limit further progression (9). Physical treatments include the use of devices like EZbite, mouth gags, heisters jaw openers, acrylic splints, and the gold fish exercise technique, all of which are aimed at stretching the mouth muscles to prevent future reductions in mouth opening. Hyperbaric oxygen therapy (HBOT) is also used to reduce proinflammatory cytokines and prevent the generation of reactive oxygen species, thereby reducing fibroblast death and limiting fibroblast activity (12). Microwave diathermy, another treatment modality, selectively heats the juxta-epithelial connective tissue to physiologically lyse fibrous bands, with ultrasound playing a crucial role in this process (13).

The role of nutrition in OSMF management is significant, as adequate intake of vitamins A, B, C, D, E, and minerals like iron, copper, calcium, zinc, and magnesium, as well as green tea with its polyphenols, can effectively reduce free radical levels. Low consumption of fruits and vegetables has been associated with a higher risk of developing pre-malignancies and cancers; thus, a diet rich in these foods is recommended to enhance antioxidant levels and reduce cancer risk (9). Laser treatments, including CO₂ lasers and other types like ErYCCG, KTP 532, and diode lasers, have been employed for their precision in removing fibrous bands, especially in the buccal mucosa (14). Cryosurgery is another technique that involves the local destruction of abnormal tissues by freezing them using liquid nitrogen or argon gas (15).

In terms of medicinal management, steroids, hyaluronidase, chymotrypsin, placental extracts, ayurvedic treatments, collagenase, and traditional Chinese medicines are frequently used. These treatments aim to suppress the inflammatory response, reduce fibroblast proliferation, and decrease collagen deposition (16). Steroids, particularly glucocorticoids and corticosteroids like hydrocortisone and dexamethasone, have a long history of use in treating OSMF. Traditional Chinese medicines, such as *Salvia/miltiorrhiza*, have shown some efficacy in OSMF treatment, and their combination with Western medicine may yield better results (17).

Surgical modalities are reserved for individuals with severe trismus, including class III and onwards. These may include fibrotomy (fibrous band incision), fibrotomy with grafts, laser treatment, and scalpel-based procedures. Each surgical technique is chosen based on the specific needs and stage of the patient's condition.

MATERIAL AND METHODS

In conducting this narrative review, a comprehensive and systematic approach was adopted to explore the various aspects of Oral Submucous Fibrosis (OSMF) and its treatment modalities. The study was designed as a narrative review, allowing for a broad and integrative examination of the literature on the subject.

The search strategy was meticulously planned to encompass a wide range of scientific databases and search engines. These included PubMed, Scopus, Web of Science, and Google Scholar, among others. The search string was carefully constructed to capture the most relevant studies. Keywords such as "Oral Submucous Fibrosis," "OSMF treatment," "areca nut," "fibrosis management," and

"oral mucosa fibrosis" were used in various combinations to ensure a comprehensive retrieval of pertinent literature. The time frame for publication was not restricted, allowing for the inclusion of both historical perspectives and the latest research findings.

The review process involved initial screening of titles and abstracts, followed by a thorough examination of full-text articles. Inclusion criteria were set to encompass studies that provided detailed insights into the pathogenesis, clinical presentation, and management of OSMF. Both primary research articles and existing review papers were considered. Exclusion criteria were applied to filter out non-English language papers, studies with insufficient data on OSMF, and articles not accessible in full text.

The evidence assessment was conducted with a focus on the quality, relevance, and contribution of each study to the understanding of OSMF. The assessment took into consideration factors such as the study design, sample size, methodological rigor, and the impact of findings on clinical practice. This evaluation helped in synthesizing a comprehensive narrative that not only presented the current state of knowledge but also identified gaps in the literature and potential avenues for future research.

Throughout the process, the review maintained an objective and unbiased approach, ensuring that the findings and discussions were solely driven by the evidence gathered. This methodological rigor was instrumental in developing a well-rounded and informative narrative review on Oral Submucous Fibrosis.

Table 1 Findings

Intervention Modality	Intervention Agents	Mode of Action	Authors
Education and Counselling	Cessation of chewing betel nuts, areca nuts, and other local irritants	Encouraging patients to stop harmful habits through education and counselling	Patil SR
Physical Therapy	EZbite, Acrylic splints, Gold fish exercise technique, HBO therapy, Microwave diathermy	Stretching exercises for mouth muscles, HBO for preventing reactive oxygen species, Diathermy for selective heating	Patil SR, Ye X, Zhang J, Lu R, Zhou G, Gupta DS
Nutritional Support and Minerals	Vitamins A, B, C, D, E, Iron, Copper, Calcium, Zinc, Magnesium, Green tea (polyphenols)	Reducing levels of free radicals and enhancing antioxidant levels to reduce cancer risk	Patil SR
Lasers	ErYCCG laser, KTP 532, Diode lasers, CO2 lasers	Providing optimal visibility and accuracy in removing fibrous bands, requiring tiny incisions for surgical relief in restricted oral aperture	Chaudhary Z, Verma M, Frame JW
Cryosurgery	Cryocautery	Freezing aberrant tissue using liquid nitrogen or argon gas to destroy it locally	Frame JW
Medical Therapy	Immunomodulatory agents (Dexamethasone, Triamcinolone acetonide, Betamethasone valerate), Antioxidants (Lycopene, Beta carotene, Alpha tocopherol), Antifibrotic cytokines (INF-gamma, Pentoxifylline, Hyaluronidase)	Suppressing inflammatory reactions, decreasing fibroblast proliferation and collagen deposition, separating free oxygen radicals and repairing their effects, altering collagen synthesis, promoting blood flow and fibrinolysis	CA. Squier, MJ. Kremer, H. Xie, J. Guo
Surgical Modalities	Fibrotomy with coronoidotomy and/or coronoidectomy, Reconstruction options (Split thickness skin graft, Nasolabial flap, Palatal flap, Lingual pedicle flap, Buccal fat pad)	Releasing fibrotic bands by incision and reconstructing the defect	Ambreen A, Gupta H, Chang Y-M, Pandya H, Surej KL
Stem Cell Therapy	Autologous bone marrow stem cells or stem cells from dental pulp	Intralesional injection to aid in angiogenesis	Sankaranarayanan Seshadri

DISCUSSION

The surgical management of Oral Submucous Fibrosis (OSMF) encompasses a range of procedures aimed at mitigating the debilitating effects of this condition. Fibrotomy, a primary surgical approach, involves the incision or removal of fibrous bands in the oral cavity, consequently forcing mouth opening. However, a significant challenge following this procedure is the frequent occurrence of relapses (18,19). To address this, adjunctive therapies like coronoidectomy and coronoidotomy are employed. Coronoidectomy entails the deliberate sectioning of the coronoid process, with or without muscle detachment, while coronoidotomy involves the intentional separation of the coronoid process from its attachment to the temporalis muscle. The primary aim of these therapies is to alleviate the pull of the temporalis muscle on the jaw during movement, thus improving mouth opening. This approach was notably effective in a study by Chang et al., where coronoidectomy was used in the treatment of patients with head and neck cancer experiencing jaw opening difficulties due to radiation therapy, showing encouraging results for OSMF patients as well (20).

Furthering the surgical intervention, the incision of fibrous bands is often followed by reconstruction using various flaps. The choice of flap is crucial, as it significantly reduces the chances of recurrence. Surgeons commonly opt for the nasolabial flap, buccal fat pad, free radial forearm flap, collagen sheet, or full-thickness skin graft to cover the raw area post-incision. The versatility of the nasolabial flap, for instance, lies in its ability to be elevated easily and its proximity to the defect, making it suitable for a range of orofacial abnormalities. It is particularly advantageous due to its flexibility, adequate size for defect coverage, and the cosmetic acceptability of the resulting scar in a natural crease, although it is generally not preferred for young females due to donor site issues. The palatal island flap is another option, used for various orofacial repairs such as the palatine arch, tonsillar fossa, retromolar trigone, and the posterior floor of the mouth. Its advantages include local accessibility, strong tensile strength, good vascularity, and a reasonable range of movement. Notably, Khanna and Andrade modified a technique using a bilateral palatal island flap in conjunction with bilateral temporalis myotomy and coronoidectomy, resulting in significant improvements in preoperative mean maximal mouth opening (25-28).

Tongue flaps, derived from the dorsolateral portion of the tongue, also play a role in reconstruction, although they occasionally become part of the OSF disease process, leading to potential postoperative complications such as dysphagia and speech issues (29,30). Bhrary et al. reported satisfactory results in OSMF patients treated with tongue flaps, a finding echoed by Tepan et al. in their study (31,32). Moreover, the use of collagen membranes in surgical management, as performed by Nataraj et al., Paramhans et al., and Farooqui et al., offers benefits such as non-antigenicity, tissue acceptability, and quick epithelization, reducing the need for more invasive flap surgeries (33-36).

Skin grafting techniques, both partial and full thickness, have been instrumental in covering defects post-fibrotomy. Yen's pioneering use of a split-thickness skin graft for the buccal defect set a precedent, followed by successful outcomes noted by Kavarana and Bhatena, and Mokal et al., in using such grafts post-temporalis myotomy and coronoidectomy (37-39). However, it's important to consider the risk of wound contracture, transplant rejection, and recurrence, especially given the reduced vascular supply in the fibrotic area, as highlighted in studies by Khanna and Andrade (40,41).

In more advanced surgical interventions, the use of free flaps, such as the radial forearm flap, represents a time-consuming and expensive strategy requiring specialized expertise. Shadamarshan R A's application of free forearm flaps for buccal mucosa repair, combined with coronoidectomy and temporal muscle myotomy, has shown promise in effectively releasing fibrotic tissue and aiding jaw opening (42).

Additionally, the latest advancements in OSMF treatment include stem cell therapy. Sankaranarayanan et al. conducted a significant study assessing the function improvement and sustainability of stem cell therapy results over a five-year follow-up, revealing substantial improvements in mucosal suppleness, reduction in burning sensation, and increased mouth opening (43). Furthermore, recent research underscores the synergistic role of omega-3 in OSMF management. Studies by Vasilev et al. (2009) and Din et al. (2013) demonstrate that omega-3 can reduce inflammation by influencing polymorphonuclear leukocytes, enhance endothelial vasomotor function, and improve microcirculation, thereby ameliorating the impaired mucosal vascularity characteristic of OSMF and increasing vasodilation (44,45).

The surgical management of OSMF is multifaceted, incorporating a range of techniques from fibrotomy and adjunctive therapies to advanced reconstructive procedures and emerging treatments like stem cell therapy and omega-3 supplementation. Each method offers unique benefits and challenges, and the choice of treatment is contingent on the individual patient's condition and the severity of OSMF.

CONCLUSION

The comprehensive review of treatment modalities for Oral Submucous Fibrosis (OSMF) underscores a multifaceted approach, integrating both traditional and innovative techniques. Surgical interventions, ranging from fibrotomy and adjunctive procedures like coronoidectomy to advanced reconstructive methods using various flaps and grafts, remain crucial in managing severe cases. The emerging treatments, such as stem cell therapy and the use of omega-3, show promising results in enhancing tissue repair and reducing inflammation, respectively. These findings suggest that a personalized treatment plan, considering the specific needs and disease stage of each patient, is imperative for effective management of OSMF. Furthermore, the continuous evolution in surgical techniques and the integration of novel therapies like stem cell treatment indicate a progressive shift towards more targeted and efficient management strategies. This highlights the need for ongoing research and development in this field to refine existing treatments and explore new avenues, potentially leading to more effective and less invasive options for patients suffering from OSMF.

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