Recent Advancements in Oral Submucous Fibrosis Management: an Overview

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Abstract
The management of Oral submucous fibrosis has been the subject of controversy ever since Schwartz first described the condition in 1952. It is a potentially malignant disorder and a crippling condition of oral mucosa. An attempt is made to update the knowledge about the management of this precancerous condition with advancements which helps to reduce the mortality of oral cancer.

Key Words: OSMF, Oral Submucous fibrosis, Management, Recent Advancements.

Introduction
In India this condition was first described as diffuse oral submucous fibrosis (Lal 1953) and as submucous fibrosis of the palate & pillars (Joshi 1953). In 1966, Pindborg defined OSMF as “an insidious chronic disease affecting any part of the oral cavity and sometimes pharynx. Although occasionally preceded by and/or associated with vesicle formation, it is always associated with juxtaepithelial inflammatory reaction followed by fibroelastic changes in the lamina propria, with epithelial atrophy leading to stiffness of the oral mucosa causing trismus and difficulty in eating.”

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Discussion
As the exact causative factor for OSMF is a matter of conflict, the failure to achieve proper or specific treatment for it may be reason for its incomplete regression. Stoppage of areca nut chewing is foremost important measure to treat OSMF. Various drugs alone or in combination are used to treat this crippling disease.

Quit Gutkha Chewing Habit & Antioxidant Supplements
Chewing Betel Quid is considered an important etiological factor of OSMF because of the excessive reactive oxygen species (ROS) induced by the ingredients of Betel Quid. Gupta et al in their study found that after 6 weeks of treatment with tablets containing mostly beta-carotene and vitamin E, patients showed an effective increase in mouth opening and tongue protrusion.

Anil & Sharma concluded that either oral zinc alone or in combination with oral vitamin A in grade I & II patients and oral zinc with local cortisone in grade III patients of OSMF may be employed in future to treat OSMF. Tai et al in their study stated the use of oral administration of milk from cows immunized with human intestinal bacteria which leads to significant improvement of symptoms and signs in OSMF patient.

Ajit had summarized various nutritional supplements (1) Micronutrients and minerals- Vitamin A, B complex, C, D and E, iron, copper, calcium, zinc, magnesium, selenium and others (2) Milk from immunized cows- 45 g milk powder twice a day for 3 months (3) Lycopene-8 mg twice a day for 2 months.

Steroid: Topical or Intralésional Injections
Several glucocorticoids are used for the treatment of OSMF such as short-acting (hydrocortisone), intermediate acting (triamcinolone), and long-acting glucocorticoids (betamethasone and dexamethasone).
They act by their anti-inflammatory activity by inhibiting the generation of inflammatory factors and increasing the apoptosis of inflammatory cells. Thereby partially relieving the patients of their symptoms at an early stage of OSF. Therefore steroids are useful in controlling symptoms, or as an adjunct therapy. A combination of Chymotripsin (5000 IU), hyaluronidase (1500 IU) and dexamethasone (4 mg), twice weekly submucosal injections for 10 weeks. Currently, intralesional steroids are the main treatment modality. These are injected into the fibrotic bands biweekly for 6–8 weeks along with mouth-opening exercises.

### Biogenic Stimulation

Placentrex is an aqueous extract of human placenta that contains nucleotides, enzymes, vitamins, amino acids, and steroids. It acts by biogenic stimulation and increasing the vascularity of tissues based on the principle of tissue therapy introduced by Filatov in 1933. Katharia reported that placenta extract when administered result in significant improvement in mouth opening, color of mucosa, burning sensation, and reduction of fibrotic bands.

### Antifibrotic Intralesional Injections

Collagenase is a lysosomal enzyme, capable of degrading phosphate esters, proteins, polysaccharides, glycosides, and sulfate esters. In a controlled clinical trial, Lin and Lin found that Intralesional injections of collagenase resulted not only in significant improvement in mouth-opening, a striking reduction of hypersensitivity to spices, sour, cold, and heat. Hyaluronidase also showed a much quicker effect in ameliorating the burning sensation and painful ulceration than did dexamethasone, though the effect was short-term. It acts by depolymerizing hyaluronic acid, which is the ground substance in connective tissue, lowering the viscosity of the intercellular cement substance, and decreasing collagen formation. Chymotrypsin, an endopeptidase, hydrolyzes ester and peptide bonds and is also used as a proteolytic and anti-inflammatory agent in the treatment of OSF.

### Vasodilator Concept

Pentoxifylline is a methylxanthine derivative that has vasodilating properties and increases the mucosal vascularity. The curative effect of pentoxifylline may be attributable to its properties of suppressing leukocyte function, altering fibroblast physiology, and stimulating fibrinolysis. Rajendran et al conducted a pilot study of Pentoxifylline therapy (Trental) 400 mg 3 times daily for 7 months and concluded as an adjunct therapy in the routine management of OSMF.

### Ayurvedic Concept

Curcuma longa Linn. is commonly known as Haldi, Turmeric or Indian saffron belongs to family Zingiberaceae. Mishra et al reported that the volatile oil of Curcuma longa has effective anti-inflammatory and anti-hyaluronidase action. They suggested the antioxidative effect as evidenced by inhibition of diffusion capability of the hyaluronidase enzyme by the oil. Ramsewk et al described in their study the cytotoxic, anti-inflammatory and antioxidant activity of curcumin I, II and III from Curcuma. Ajit reported the use of alcoholic extracts of turmeric (3g), turmeric oil (600mg), turmeric oleoresin (600mg) daily for 3 months as a treatment modalities for oral sub mucous fibrosis patients.

### Natural Supplements Concept

Tea pigments are oxidized products of polyphenols, derived from tea leaves that could improve microcirculation and hemorrheology. After administering tea-pigment tablets in the treatment of OSF, Li and Tang found an overall effective rate and believed that tea pigment’s acts by decreasing high blood viscosity, improving microcirculation, and increasing the activity of superoxide dismutase.

### Surgical Concept

The various surgical modalities chosen according to the stage of clinical progression to gain maximal interincisal distance (ID) includes the excision of fibrotic tissues and covering the defect with split-thickness skin, fresh human amnion, or buccal fat pad (BFP) grafts. Khanna & Andrade treated advanced cases by a new surgical technique of a palatal island flap based on the greater palatine artery in combination with temporalis myotomy and bilateral coronoidectomy.

### Stem Cell Intra-leisonal Injections Concept

It is an alternative approach to improve the blood circulation Sankaranarayanan et al injected autologous bone marrow stem cells in 38 year old male patient with oral submucous fibrosis which showed significant improvement in blanching, fibrous bands and mouth opening, 4 weeks after injection.

### Physical Exercise Concept

Stephen & Hans conducted a clinical trial of Physiotherapeutic treatment to improve oral opening in oral submucous fibrosis in the Nepali population and suggested that physiotherapy is effective for increasing the oral opening and can be readily used to improve OSF in communities with otherwise limited health resources.
Mucoadhesive Patch Concept
Averineni et al conducted a preliminary study to develop mucoadhesive buccal films of valdecoxib a novel COX-2 inhibitor for the treatment of oral sub-mucous fibrosis. 17

Laser Concept
Jawahar & Talsania et al evaluated the efficacy of Laser with follow-up physiotherapy to reduce trismus in OSMF and concluded that Diode laser is a less expensive and an alternative method in Asian population as it requires less hospital stay and less follow up as compared to other surgical methods. 18

Conclusion
As long time span of time has been passed since first diagnosis of OSMF and treatment given for it till this era, no complete success has been achieved. Reason for this may be the unpredictable etiology, immune response or immune status of individual patient, and pro and cons of every treatment modality depending on the stage of the OSMF. After having a glance over the vast literature on OSMF, it is said that there is hope for further detail evaluation for management of OSMF for having better outcome results to the patients suffering from this precancerous condition.

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