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Submucous Fibrosis: A Review of Current Literature on a Etiopathogeneses. Diagnosis, Treatment and Prosthetic Rehabilitation.

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Abstract

Oral Submucous fibrosis (OMF), a premalignant condition is marking its presence in India and its subcontinent population extensively. Due to the use of betel nuts and Gutkha and addiction to them, OMF is becoming uncontrolled. Although its chances of malignancy have been reported very rare, but the effects of OMF at the late stages on an individual is severe and irreparable. Scholars have been successfully highlighted upon the etiopathogenesis of this condition. Burning mouth and trismus makes difficulty for patients to eat. The main challenge is proper examination and treatment of intra oral lesions and tooth related symptoms. There have been various types of approach to treat OMF and new techniques have evolved for Prosthodontic management.

Many literature are present on OMF, but none on detailed and comprehensive surgical and non-surgical management that includes the role of Prosthodontists. This review article summarizes the premalignant condition of OMF, from its diagnosis, its etiopathogenesis to treatment and recent advances in its prosthetic management.

Keywords: *Oral submucous fibrosis, Prosthodontic management of oral submucous fibrosis, curcumin in oral submucous fibrosis*

Introduction

Oral submucous fibrosis (OMF) is a potentially malignant condition of the oral cavity characterized by juxtraepithelial inflammatory reaction and progressive fibrosis of the lamina propria and deeper connective tissues of the upper digestive tract involving the oral cavity, oropharynx and frequently the upper third of the oesophagus. OMF results in an increasing loss of tissue mobility marked rigidity and an eventual inability to open the mouth. [1,2]

It was first reported by Schwartz in 1952 among five Indian females from Kenya and he designated the term 'Atropica Idiopathica Mucosae Oris' to this condition. In 1953, Joshi described this condition as 'submucous fibrosis'. [3–5] A condition resembling OMF was described as early as 600 BC by Sushruta and it was named as 'VIDARI' having features of progressive narrowing of mouth, depigmentation of oral mucosa and pain on taking food.[6]

Aetiology

A variety of etiologic factors including capsaicin, betel nut alkaloids, hypersensitivity, autoimmunity, genetic predisposition and chronic iron and vitamin B-complex deficiency have been suggested by various authors, the most common of which is chewing areca nut. [7–11] Excessive use of areca nut may cause fibrosis due to increased synthesis of collagen and induction of free radicals and reactive oxygen species, which are responsible for a high rate of oxidation/peroxidation of polyunsaturated fatty acids which affect essential constituents of the cell membrane and might be involved in tumorigenesis.[12,13]

The role of chilli (Capsicum annum and Capsicum frutescence) ingestion in the pathogenesis of oral submucous fibrosis is controversial. A hypersensitivity reaction to chillies is believed to contribute to oral submucous fibrosis.[2] Epidemiological studies have clearly shown that the regular use of areca nut is the major etiological factor of OMF.[14]

Epidemiology

Approximately 600 million persons are betel chewing, with a hot spot throughout the Western Pacific basin and South Asia. This makes betel the fourth most-consumed drug after nicotine, ethanol, and caffeine.[15,16] Betel is composed of the areca nut (*Areca catechu*), the fresh leaf of betel pepper (*Piper betel*), spices, and calcium hydroxide (lime). Pan or pan masala is a quid of piper betel leaf.[17] Mawa is a mixture of tobacco, lime, and areca nut. Chewing tobacco or *gutkha* is very popular in the Indian subcontinent, and betel chewers often use *gutkha* as an adjunct. However, *gutkha* has recently been officially banned in many Indian states but overall, chewing tobacco-containing betel quid has become more popular in South Asia.[18–21] Since there is a lot in common between the various areca nut mixtures (pan, mawa) we will not attempt to differentiate between them. Betel is now widely available in the Western world as well.[22] OMF subjects are younger and have shorter histories of chewing

compared to chewers without OMF. Once established, OMF does not regress or disappear following cessation of the habit.[23]

A study from the state of Gujarat in India has shown that the prevalence of OMF is increasing – from 0.16% in 1967 to 10.9% in 1998. About 85% of patients were younger than 35 years.[19] In 2005, this disease's prevalence among visitors at a dental school in Manipal, India was estimated at 2%, with a preference for male sex and an age range of 40–60 years. [24] The prevalence of OMF in an aboriginal community of southern Taiwan was 17.6%. Although the betel quid in Taiwan does not contain any tobacco, in contrast to India and Pakistan, a significant association with oral mucosal lesions was still identified.[25]

In a study of 239 OMF patients from Allahabad, India, 46% were in their 3rd decade of life. The most common affected subsite was buccal mucosa (20.8%), followed by the palate (17.7%). Trismus was observed in 37.2% of patients, 25.9% suffered from burning sensation, 22.5% reported excessive salivation, and 14.2% suffered from recurrent oral ulcerations. [26]

Grading OMF with addiction habits demonstrated a dependence from years of addiction and the frequency of chewing betel and tobacco. Most patients with stage I OMF were addicted for at least 3–5 years, whereas the majority of patients with stage III OMF had consumed betel and tobacco products for 8–10 years or more with a frequency of 6–10 times per day. Trismus was seen more often in stage II and III OMF, but a clear correlation between the severity of trismus and OMF staging was missing.[26]

Diagnostics

The hallmark of diagnosing OMF is clinical and histological. Clinically, one or more of the following symptoms should be present:

• Blanching of oral mucosa defined as a persistent, white, marble-like appearance of the oral mucosa, which may be localized, diffuse or reticular

• Tough, leathery texture of the mucosa

• Palpable, whitish, fibrous bands.

A clinical diagnosis is confirmed by histopathological interrogation. OMF is characterized by epithelial atrophy with loss of rete ridges and hyalinization of the lamina propria and the underlying muscle.[27]

The initial pathology of OMF is characterized by mixed inflammation and oedema, and large fibroblasts. Later, collagen bundles with early hyalinization are seen, and the inflammatory infiltrate contains lymphocytes and plasma cells, occasionally resembling lichenoid mucositis.[28]

In more advanced stages, OMF is characterized by the formation of thick bands of collagen and hyalinization extending into the submucosal tissues and decreased vascularity. The epithelium becomes thinner or hyperkeratotic. Inflammation and fibrosis of minor salivary glands may develop. Muscle degeneration is demonstrated in advanced stages of OMF.[29,30] In vivo autofluorescence from buccal mucosa appears to be an interesting non-invasive tool to differentiate normal mucosa from OMF and early carcinoma.[29]

Classification

Several classifications have been proposed by various authors. However, none of them find universal application with regards to description of morphology or in decision making for treatment.

While some authors have classified OMF based on clinical features, [30–35] others have classified the severity of disease on the extent of mouth opening, [35–38] extent of mucosal area involvement [39] and histopathological characteristics [31,38,40–43]

The reader is directed to the above references for a detailed basis of these classifications.

• JV Desa [44] in 1957 divided OMF into three stages as follows:

– Stage I: Stomatitis and vesiculation

– Stage II: Fibrosis

– Stage III: As its sequelae

• Pindborg JJ [7] in 1989 divided OMF into three stages as follows:

– Stage I: Stomatitis includes erythematous mucosa, vesicles, mucosal ulcers, melanotic mucosal pigmentation and mucosal petechiae.

– Stage II: Fibrosis occurs in healing vesicles and ulcers, which is the hallmark of this stage.

- Early lesions show blanching of the oral mucosa.

- Older lesions include vertical and circular palpable fibrous bands in the buccal mucosa and around the mouth opening or lips.

- This results in a mottled marble-like appearance of the mucosa because of the vertical thick, fibrous bands in association with a blanched mucosa.

- Specific findings include reduction of mouth opening, stiff and small tongue, blanched and leathery floor of the mouth, fibrotic and depigmented gingiva, rubbery soft palate with decreased mobility, blanched and atrophic tonsils, shrunken bud-like uvula and sunken cheeks, not commensurate with age or nutritional status.

– Stage III: Sequelae of OMF are as follows:

- Leukoplakia is found in more than 25% of individuals with OMF.

- Speech and hearing deficit may occur because of the involvement of the tongue and the Eustachian tube.

• SK Katharia et al [33] in 1992 have given different scores assigned to the patients based on mouth opening between upper and lower central incisors as follows:

– Score 0: Mouth opening is 41mm or more

– Score 1: Mouth opening is 37 to 40 mm

– Score 2: Mouth opening is 33 to 36 mm

– Score 3: Mouth opening is 29 to 32 mm

– Score 4: Mouth opening is 25 to 28 mm

– Score 5: Mouth opening is 21 to 24 mm

– Score 6: Mouth opening is 17 to 20 mm

– Score 7: Mouth opening is 13 to 16 mm

– Score 8: Mouth opening is 09 to 12 mm

– Score 9: Mouth opening is 05 to 08 mm

– Score 10: Mouth opening is 0 to 04 mm.

• Lai DR [45] in 1995 divided OMF based on the interincisal distance as follows:

– Group A: >35 mm

– Group B: Between 30 and 35 mm

– Group C: Between 20 and 30 mm

– Group D: <20 mm

• R Maher et al [34] in 1996 has provided criteria for evaluation of interincisal distance as an objective criterion of the severity of OMF in Karachi, Pakistan. In his study, he divided intraoral regions into eight anatomical subregions viz palate, posterior one-third of buccal mucosa, mid-one-third of the buccal mucosa, anterior one-third of buccal mucosa, upper labial mucosa, tongue and floor of the mouth and looked for disease involvement in each to assess the extent of clinical disease. This was further grouped into three categories as follows:

– Involvement of one-third or less of the oral cavity (if three or less of the above sites are involved).

– Involvement of one to two-thirds of the oral cavity (if four to six intraoral sited are involved).

– Involvement of more than two-thirds of the oral cavity (if more than six intraoral sites are involved).

• Ranganathan K et al [32] divided OMF based on mouth opening as follows:

– Group I: Only symptoms, with no demonstrable restriction of mouth opening.

– Group II: Limited mouth opening 20 mm and above.

– Group III: Mouth opening less than 20 mm.

– Group IV: OMF advanced with limited mouth opening. Precancerous or cancerous changes seen throughout the mucosa.

• Rajendran R [10] in 2003 reported the clinical features of OMF as follows:

– Early OMF: Burning sensation in the mouth. Blisters especially on the palate, ulceration or recurrent generalized inflammation of oral mucosa, excessive salivation, defective gustatory sensation and dryness of the mouth.

– Advanced OMF: Blanched and slightly opaque mucosa, fibrous bands in buccal mucosa running

in a vertical direction. Palate and faucial pillars are the areas first involved. Gradual impairment of tongue movement and difficulty in mouth opening.

Treatment Options

Many researchers have worked upon and elucidated the etiopathogenesis of OMF. The main symptoms of oral submucous fibrosis include burning sensation, difficulty to eat and trismus. The treatment of patients with OMF depends on the degree of clinical involvement. Management of OMF has been tried by both surgical and non-surgical approach.

I Conservative treatment - Conservative treatment includes restriction or avoidance of high-risk habits, nutritional or supportive therapy and oral physiotherapy.

a. Restriction of habits - The consumption of chillies, pan, areca nut, spices and commercially available gutkha and pan masala is increasing in India. Patient motivation to quit the habit in the early stage of OMF has been seen to slow the progress of the disease. [46]

b. Nutritional or supportive therapy - Micronutrients and minerals such as vitamin A, B, C, D and E, iron, copper, calcium, zinc, magnesium, and selenium were demonstrated to diminish the oxidant levels. Low ingestion of fruits and vegetables has also been linked to an increased risk of developing pre-cancers and cancers. [47]

Polyphenols in green tea have proven radical scavenging activity and can protect cells from DNA damage caused by reactive oxygen species and also hinders tumour cell proliferation and induces apoptosis. Thus, many of the potential beneficial special effects of tea on OMF have been ascribed to the strong antioxidant activity of tea polyphenols. [48]

Various studies have been associated with the deficiency of iron both as a cause and consequence, in the etiopathogenesis of OMF. Thus, routine assessment of haemoglobin levels followed by iron supplements are being incorporated in treatment plans. [49]

Immune milk has a high-quality anti-inflammatory effect and contains a reasonable amount of vitamins such as A, B1, B2, B6, B12, C, pantothenic acid, nicotinic acid, folic acid, iron, copper and zinc. Presence of IgG antibody in immunised milk has been shown to restrain inflammatory reactions and modulates cytokine assemblage in OMF patients, which is believed to contribute to clinical improvement. [50]

c. Oral physiotherapy - Physiotherapy in OMF is administered in the form of a physical exercise regimen or by using splints and other devices. Muscle stretching exercises intended for the mouth may be supportive to prevent further limitation of jaw opening. Slow stretching of the fibrous bands is achieved with these exercises. Forceful mouth opening has been tried with mouth gag and acrylic surgical screw [39] followed by the maintenance of achieved mouth opening by devices like ice cream sticks, Heister's mouth gag & Therabite®.

d. Microwave diathermy - Heat therapy acts by fibrinolysis of bands. Microwave diathermy selectively heats only juxta-epithelial connective tissue and limits the area to be treated. Thus, it is accepted with minimum discomfort. [39]

II Medical Treatment

Treatment includes intra-lesional injection of steroids, Placentrex® and fibrinolytic agents. Medical treatment is symptomatic and intended at improving the mobility of tissues.

a. Steroids - Steroids are well recognized as immunosuppressive agents causing inhibition of inflammation seen in OMF lesions. Besides, steroids slow down the proliferation of fibroblasts and reduces the number of collagen fibres. [51]

Sub-mucosal intra-lesional injections given weekly or topical application of steroids in patients with moderate OMF may help to avoid incremental damage. Steroid ointments applied topically may be helpful in ulcers and in painful oral mucosal lesions.

b. Hyaluronidase - In vitro studies, suggest that hyaluronidase acts faster on collagen in OMF compared to normal collagen. Hyaluronidase degrades the hyaluronic acid matrix, lowers the thickness of intracellular cemental substance and activates definite plasmatic mechanisms. As a result, it causes softening and diminution of fibrous tissue. [52] Kakar et al. found that injection of 1500 IU of hyaluronidase and dexamethasone (4 mg) locally for 7 weeks gave superior results if it was followed by 3 weeks of hyaluronidase injections. [53]

c. Collagenase - Reduced content of functional collagenase observed in OMF patients is one of the mechanisms accountable for collagen accumulation. Lin and Lin found that intra-lesional collagenase injections not only resulted in improvement of mouth opening, but patients also experienced a striking decline in hypersensitivity to spices, cold, and heat .[54]

d. Placental extracts- The injection Placentrex® is an aqueous extract of human placenta containing nucleotides, enzymes, amino acids, steroids and vitamins. It acts by “biogenic stimulation”. Filatov introduced its use in 1933. Such tissues or their extracts, implanted or injected into the body are believed to stimulate metabolic or regenerative processes, thereby favouring recovery. [55]

e. Chymotrypsin: Chymotrypsin is an endo-peptidase enzyme that can execute proteolysis.

Interferon (IFN)-gamma IFN-gamma plays a significant role in the treatment of OMF for the reason that it has an immunoregulatory effect. Haque et al. studied the antifibrotic effects of IFN-gamma on collagen synthesis using arecoline stimulated OMF fibroblasts. IFN-gamma intra-lesional injection was seen to improve in mouth opening in this trial. [42]

f. Aloe vera

Aloe vera foliage, extract and resin present anti-microbial, anti-inflammatory and healing properties. Sudarshan et al. have carried out a preliminary study to contrast the efficacy of A. vera with antioxidants in the treatment for OMF. Results of this study showed that A. vera response was enhanced in all the parameters evaluated and the subset of patients with mild- stage clinically and early-stage histopathologically benefited most prominently. Use of A. vera also showed a decline in burning sensation, improvement in mouth opening and cheek flexibility. It was concluded that A. vera group reduces the burning sensation and recovers mouth opening, enhancing the patient's quality of life. [43]

g. Turmeric

Curcumin (diferuloymethane) found in turmeric, a natural yellow pigment exhibits anti-oxidant, anti-inflammatory and anti-cancer properties. Turmeric oil and turmeric oleoresin together offer defence against DNA damage. As such, it may serve to fulfil two roles in the putative treatment of OMF, both as an anti-inflammatory agent and as a chemo-preventive agent. It also provides a base for a simple, safe, acceptable and cost-effective intervention for earlier stages of OMF. Rai et al also conducted a study using curcumin in the treatment of oral precancerous lesions. 25 patients of OMF were included and these patients were cured by curcumin. [56]

Pharmacological Properties of Curcumin

Curcumin (1,7-bis (hydroxyl-3-methoxyphenyl) -1,6-heptadiene-3,5-dione), is one of the most extensively investigated drugs for submucous fibrosis. Curcumin is insoluble in water, but soluble in ethanol and acetone. The naturally occurring ratios of curcuminoids in curcumin are about 5% bisdemethoxycurcumin, 15% demethoxycurcumin, and 80% curcumin.[57] The various components of the turmeric have their medical importance.

Apart from its anti-inflammatory effects, including inhibition of COX 2, curcumin also demonstrated antioxidant, antiangiogenic, antiproliferative, and apoptotic activity. It has also been shown as acting as an inhibitor of cell adhesion and metastasis.

It was found that curcumin mediates its anti precancer activities by increasing levels of vitamins C and E and preventing lipid peroxidation and DNA damage. This could be due to curcumin-induced production of vitamins C and E and preventive DNA damage by decreasing the oxidation stress. This suggests that the anti-precancerous effects of curcumin are mediated through pro-oxidant and anti-oxidant pathways. [58] Another study showed that the use of curcumin in OMF significantly reduced connective tissue growth factor which prolonged the onset and progression of OMF. [59]

This combination of anti-inflammatory and antitumour properties of curcumin has directed research in the direction of its potential application in the treatment of OMF.

Curcumin Role in Oral Submucous Fibrosis

A wide range of treatment modalities have been proposed for OMF, but none have been proved to be curative, so the search for effective treatment modality continues. Plants have been a major source of medicine since the time immemorial. Various studies have been conducted worldwide to show the therapeutic effect of curcumin on OMF.

Agarwal N et al. conducted a study to check the efficacy of turmeric in 30 OMF patients. An improvement in mouth opening and burning sensation was noticed.. [60]

Another study conducted by Deepa DA et al., to evaluate the efficacy of curcumin and turmeric dispensed in two forms namely curcumin capsules and turmeric oil in 48 patients with OMF. Statistically, significant improvement was observed in the clinical signs and symptoms of patients treated with curcumin and turmeric oil. [61]

Yadav M et al. conducted a study for comparison of curcumin with intralesional steroid injections in OMF patients. Improvement of burning sensation, interincisal distance and tongue protrusion was evaluated weekly and it was found that there was a marked improvement in burning sensation, intraincisal distance and tongue protrusion. [62]

Balwant Rai conducted a study to know the possible mechanism of action for curcumin in pre-cancerous lesions and condition based on serum and salivary markers of oxidative stress. [56]

h. Pentoxifylline therapy

Pentoxifylline is a methylxanthine derivative that produces dose-related effects. It has been known to act in following possible ways:

1. Improvement of microcirculation and reduction of platelet aggregation and granulocyte adhesion.

2. Leukocyte deformability is amplified with retardation of neutrophil adhesion and activation. It also has anti-thrombin, anti-plasmin, and fibrinolytic activity.

3. Degranulation of neutrophils and increase in natural killer cell activity and inhibition of T and B-cell activation.

4. Maintains cellular integrity and homeostasis following acute injury. [55]

Rajendran et al. used pentoxifylline as an accessory drug in OMF treatment and after 7 months of intervention and 6-12 months of follow-up, the patients showed improvement in signs and symptoms as compared to controls. [63]

III Surgery

It is the technique of choice in patients with limited mouth opening and/or biopsy showing dysplastic or neoplastic changes. It includes:

a) Fibrotomy

b) Fibrotomy with grafts

c) Laser treatment

d) Mononuclear Stem Cell Therapy

a) Fibrotomy- The surgical treatment involves excision of fibrous bands and forceful mouth opening resulting in a raw wound. Relapse is a common complication that occurs after surgical release of the oral trismus caused by OMF. [54]

b) Fibrotomy with grafts- The principle behind all surgical procedures is an incision (incorrectly termed as excision) or surgical release of fibrous bands followed by the forceful opening of the mouth (widening of the incised tissue or region) and covering of surgical defects using various flaps or synthetic biological material. [64]

c) Extra-oral flaps- like Split thickness skin graft. [64], superficial temporal fascia pedicled flap. [65] ,nasolabial flap. [66], platysma myocutaneous muscle flap. [67] have also been described with varying success.

d) Intraoral flaps - Tongue flap, Palatal island flap, Buccal fat pad [68] have also been described but no compelling evidence points to their use

e) Microvascular free flaps like the radial forearm free flap, anterolateral thigh flap [69] have been described as case reports

f) Alloplasts - Collagen membrane, Artificial dermis [70]

g) Laser treatment: Lasers offer oral surgeons with a new modality for treating OMF. The erbium chromium yttrium scandium gallium garnet (Er Cr: YSGG) laser has a wavelength of 2780 nm is well

absorbed by water and is used on oral soft tissue without creating thermal damage. The overall advantage of laser surgery includes a somewhat bloodless operative field and thus outstanding visibility, reduced need for local anaesthesia, less probability of bacterial infection, reduced mechanical tissue trauma, fewer sutures, quicker healing, reduced post-operative oedema, scarring and tissue shrinkage. Chaudhary et al. highlight the attempt in treating a moderate case of bilateral OMF with Er Cr: YSGG laser showed a better result during follow-up. [71]

h) Mononuclear Stem Cell Therapy: Sankaranarayanan et al. in 2013 conducted a study to assess the effectiveness of stem cell therapy in the treatment of OMF by evaluating the improvement in function and to assess the sustainability of the result with 5 years follow-up. Out of seven patients, three were treated with stem cells obtained by Ficoll method and four patients were treated with stem cells obtained by point of care delivery system. Post-treatment improvement in the clinical presentation was assessed and confirmed by histopathological features. The range of follow- up of cases was from 6 months to 5 years. Reduction in blanching, improved elasticity of mucosa, decrease in burning sensation while consuming spicy food, increase in mouth opening was observed. The above results were found to be sustained in the follow-up period. [40]

PROSTHODONTIC MANAGEMENT

Prosthetic rehabilitation of patients with OMF present difficulties at all stages, right from making the preliminary impressions till the fabrication and insertion of the final prosthesis due limited mouth opening in these patients.

Types of trays

Sectional stock tray for preliminary impressions

Prosthetic rehabilitation in an OMF patient is challenging. In each case, individual variables, such as the size and shape of the existing dental arch, position and state of the remaining teeth, and residual ridge resorption may impair the acquisition of preliminary impression with a conventional stock tray. [72].

Quality diagnostic casts and a well-fitted stock tray are critical for treatment planning in OMF patients with restricted mouth opening. Although there are individual anatomic discrepancies, this system allows different combinations of tray sizes and forms to be assembled into an anatomically well-fitted conforming tray. Modifications of conventional techniques include the usage of stock impression trays on each side of the mouth for sectional impressions with heavy- and light-body silicone impression

materials as well as with a combination of the two. For primary impressions, flexible impression trays made using silicone putty or modelling plastic impression compound can be used for making sectional impressions. The two separate parts of the sectional custom tray are inter-connected with hinges, plastic building blocks, orthodontic expansion screws or locking levers connected only at the handle. [73]

Challenges. Dental practitioners have encountered several problems with the use of sectional trays during the fabrication and placement of prostheses. When the strength of the connecting midline joint is inadequate, the impressions taken can become deformed. Polyether and polyvinyl siloxane are elastic impression materials that are self-adherent, and, when used for sectional placement, they require intraoral mechanical separation. To overcome the challenges associated with sectional impression procedures, dissimilar materials such as irreversible hydrocolloid materials that are non-adherent can be used. The two separate halves of the elastic impression materials may be inserted and removed successfully. This system is currently under trial and is not yet commercially available. [74]

Final impression. To minimize errors in the impressions that are caused by manipulation distortion after setting, a medium or light viscosity elastomeric impression material can be used.

Flexible impression trays

To make an accurate diagnostic cast, a non-rigid, flexible tray may be used along with silicon putty impression material that can be moulded within the mouth before it sets. The insertion and removal are easier in these cases as the silicon trays are flexible. Materials such as reversible and irreversible hydrocolloids, elastomeric impression materials, border moulding materials such as modelling plastic, vinyl polysiloxane and polyethers can be used. The ease of manipulation of the material, accurate placement of the material onto the ridges/borders, and multiple insertion and removal of the border-moulded impression tray can be reduced/eliminated. The definite accuracy and elimination of the use of a water bath give elastomeric materials an advantage over impression compounds. [74]

Mandibular swing-lock complete dentures

Collapsible mandibular swing-lock dentures with a cast cobalt-chromium framework, a lingual hinge and a conventional labial swing-lock can be used for prosthetic rehabilitation in OMF patients with restricted mouth opening. This helps these prostheses to be collapsible and maintain

their structural durability. They are easy to insert and remove and provide maximum coverage for good support, retention and stability. [73,75]

Sectional complete denture with cast magnetic attachments

Sectional complete dentures consist of two left and right sections that are joined with an acrylic resin overlay to connect the four studs. These prostheses restore esthetics but cause a little discomfort due to restricted tongue space.

Excellent adhesion and attractive force can be achieved using Fe-Pt dental magnetic attachments and are clinically very useful. Commercially available prefabricated dental magnetic systems are available in several sizes. A castable magnetic attachment of any size or shape can be fabricated by casting it in a dental casting machine. These attachments are either placed on the root canal of the abutment tooth or implant abutment and rigidly connect the anterior segment to the posterior segment with its concavo-convex design. This prevents the wearing of magnetized components, averts denture deflection and decreases stress concentration at the lingual or palatal midline hinge during masticatory functions, thus minimizing breakage. [73]

Graft stabilizing clip. In OMF patients undergoing surgery to correct mouth opening, Le and Gornitsky tried to use graft-stabilizing clips (GSCs) as oral stents for 6 months to prevent the relapse of the corrected mouth opening. This is a simple design that is easy to fabricate and ensures the positive contact of the graft with the recipient site. GSCs are a removable appliance that can be worn, removed and cleaned easily by the patient, making a periodic examination of the surgical site possible. [73,76]

Postoperative oral physiotherapy aid for edentulous OMF patients. Achieving optimal mouth opening with the application of interocclusal forces forms an integral part of the treatment of OMF patients. Many oral physiotherapy aids, from wooden spatulas to mouth gags (such as Heister or Ferguson), are currently in use. In edentulous OMF patients, there is a transmission of the forces to the atrophic ridges, which can cause soft tissue injuries and fractures of these aids. As an adjunct to surgeries, custom-made occlusal splints with grooves are also advisable. Dentures with added occlusal rims help with maintaining normal mouth opening without requiring any patient compliance as they are to be worn only during physiotherapy sessions. These appliances are economical, comfortable and easy to maintain. After effective tissue healing, conventional dentures can be given. [73,77]

Mouth-exercising device. Mouth-exercising devices (MED) have been introduced to increase elasticity by squeezing or stretching the buccal mucosa in OMF patients. These devices can be used alone or in combination with other treatment modalities, such as drug therapies and surgery. In mature scars, physiotherapy triggers the loosening of the thick fibrous tissue, causing the separation of collagen fibres from each other by pulsed ultrasound, which leads to increased pliability.[78,79]

Conclusion:

Exact aetiological factors are still unknown, but possible etiologies include capsaicin, betel nut alkaloids and chronic vitamin B complex and iron deficiency.

OMF presents initially as inflammation and oedema of the affected tissues followed by changes which resemble lichenoid mucositis and evolves int more advanced stages with the formation of thick bands of collagen. The epithelium thins out and becomes hyperkeratotic. Many surgical and medical interventions have been proposed but none have found universal acceptability or use. Both surgical and conservative mode of treatments are temporary or act as a primer to physiotherapy. Devices like Orabite, ® Therabite® are available to improve the mouth opening.

References

1. Warnakulasuriya S, Johnson NW, Van Der Waal I. Nomenclature and classification of potentially malignant disorders of the oral mucosa. J Oral Pathol Med 2007. https://doi.org/10.1111/j.1600-0714.2007.00582.x.

2. Aziz SR. Oral submucous fibrosis: an unusual disease. J N J Dent Assoc 1997.

3. Ahmad M, Ali S, Ali A, Chaubey K. Epidemiological and etiological study of oral submucous fibrosis among gutkha chewers of Patna, Bihar, India. J Indian Soc Pedod Prev Dent 2006. https://doi.org/10.4103/0970-4388.26022.

4. More CB, Das S, Patel H, Adalja C, Kamatchi V, Venkatesh R. Proposed clinical classification for oral submucous fibrosis. Oral Oncol 2012. https://doi.org/10.1016/j.oraloncology.2011.10.011.

5. Yusuf H, Yong SL. Oral submucous fibrosis in a 12-year-old Bangladeshi boy: A case report and review of literature. Int J Paediatr Dent 2002;12:271–6. https://doi.org/10.1046/j.1365-263X.2002.00373.x.

6. More CB, Ansari M, Patel H. Oral submucous fibrosis - a hospital based retrospective study-Indian Journals. Pearldent 2010;1.

7. Pindborg JJ. Oral submucous fibrosis: A review. Ann Acad Med Singapore 1989;18:603–7. https://doi.org/10.21474/ijar01/6351.

8. Shiau YY, Kwan HW. Submucous fibrosis in Taiwan. Oral Surgery, Oral Med Oral Pathol 1979;47:453–7. https://doi.org/10.1016/0030-4220(79)90128-2.

9. Canniff JP, Harvey W, Harris M. Oral submucous fibrosis: Its pathogenesis and management. Br Dent J 1986;160:429–34. https://doi.org/10.1038/sj.bdj.4805876.

10. Rajendran R, Vasudevan DM, Vijayakumar T. Serum levels of iron and proteins in oral submucous fibrosis (OSMF). Ann Dent 1990.

11. Gupta DS, Gupta M, Oswal RH. Estimation of major immunoglobulin profile in oral submucous fibrosis by radial immunodiffusion. Int J Oral Surg 1985;14:533–7. https://doi.org/10.1016/S0300-9785(85)80060-0.

12. Chang YC, Hu CC, Tseng TH, Tai KW, Lii CK, Chou MY. Synergistic effects of nicotine on arecoline-induced cytotoxicity in human buccal mucosal fibroblasts. J Oral Pathol Med 2001. https://doi.org/10.1034/j.1600-0714.2001.030008458.x.

13. Manoharan S, Kolanjiappan K, Suresh K, Panjamurthy K. Lipid peroxidation & antioxidants status in patients with oral squamous cell carcinoma. Indian J Med Res 2005.

14. Harvey W, Scutt A, Meghji S, Canniff JP. Stimulation of human buccal mucosa fibroblasts in vitro by betel-nut alkaloids. Arch Oral Biol 1986. https://doi.org/10.1016/0003-9969(86)90112-3.

15. Nelson BS, Heischober B. Betel nut: A common drug used by naturalized citizens from India, Far East Asia, and the South Pacific Islands. Ann Emerg Med 1999. https://doi.org/10.1016/S0196-0644(99)70239-8.

16. Zain RB. Cultural and dietary risk factors of oral cancer and precancer - A brief overview. Oral Oncol 2001. https://doi.org/10.1016/S1368-8375(00)00133-0.

17. Merchant A, Husain SSM, Hosain M, Fikree FF, Pitiphat W, Siddiqui AR, et al. Paan without tobacco: An independent risk factor for oral cancer. Int J Cancer 2000. https://doi.org/10.1002/(SICI)1097-0215(20000401)86:1<128::AID-IJC20>3.0.CO;2-M.

18. Chaudhry K. Is pan masala-containing tobacco carcinogenic? Natl Med J India 1999.

19. Gupta PC, Sinor PN, Bhonsle RB, Pawar VS, Mehta HC. Oral submucous fibrosis in India: A new epidemic? Natl Med J India 1998.

20. Roy R. Taxes make cigarette firms huff and puff. , 12 (17): February 3, 2002, p 1. - Google Search. The Sunday Times of India 2002:1.

21. Heck JE, Marcotte EL, Argos M, Parvez F, Ahmed A, Islam T, et al. Betel quid chewing in rural Bangladesh: Prevalence, predictors and relationship to blood pressure. Int J Epidemiol 2012. https://doi.org/10.1093/ije/dyr191.

22. Norton SA. Betel: Consumption and consequences. J Am Acad Dermatol 1998;38:81–8. https://doi.org/10.1016/S0190-9622(98)70543-2.

23. VanWyk CW. Oral submucous fibrosis. The South African experience. Indian J Dent Res 1997.

24. Mathew A, Pai K, Sholapurkar A, Vengal M. The prevalence of oral mucosal lesions in patients visiting a dental school in Southern India. Indian J Dent Res 2008. https://doi.org/10.4103/0970-9290.40461.

25. Yang Y-H, Lee H-Y, Tung S, Shieh T-Y. Epidemiological survey of oral submucous fibrosis and leukoplakia in aborigines of Taiwan. J Oral Pathol Med 2001;30:213–9. https://doi.org/10.1034/j.1600-0714.2001.300404.x.

26. Pandya S, Chaudhary AK, Singh M, Singh M, Mehrotra R. Correlation of histopathological diagnosis with habits and clinical findings in oral submucous fibrosis. Head Neck Oncol 2009;1:10. https://doi.org/10.1186/1758-3284-1-10.

27. Haider SM, Merchant AT, Fikree FF, Rahbar MH. Clinical and functional staging of oral submucous fibrosis. Br J Oral Maxillofac Surg 2000;38:12–5. https://doi.org/10.1054/bjom.1999.0062.

28. Lee CK, Tsai MT, Yang CC, Chiang CP. Clinical diagnosis of oral submucous fibrosis with optical coherence tomography. 2009 Asia Commun. Photonics Conf. Exhib. ACP 2009, 2009. https://doi.org/10.1117/12.852410.

29. Shafique K, Mirza SS, Vart P, Memon AR, Arain MI, Tareen MF, et al. Areca nut chewing and systemic

inflammation: Evidence of a common pathway for systemic diseases. J Inflamm (United Kingdom) 2012;9:22. https://doi.org/10.1186/1476-9255-9-22.

30. Auluck A, Hislop G, Poh C, Zhang L, Rosin MP. Areca nut and betel quid chewing among South Asian immigrants to Western countries and its implications for oral cancer screening. Rural Remote Health 2009;9:1118.

31. Tupkari, Bhavthankar J, Mandate M. Oral Submucous Fibrosis (OSMF) : A study of 101 cases. J Indian Acad Oral Med Radiol 2020;19:311.

32. Kannan R. An overview of classification schemes for oral submucous fibrosis | Request PDF. J Oral Maxillofac Pathol 2006:181–3. https://www.researchgate.net/publication/284831033_An_overview_of_classification_schemes_for_oral_submucous_fibrosis (accessed December 29, 2020).

33. Katharia SK, Singh SP, Kulshreshtha VK. THE EFFECTS OF PLACENTA EXTRACT IN MANAGEMENT OF ORAL SUBMUCOUS FIBROSIS. vol. 24. 1992.

34. Mäher R, Sankaranarayanan R, Johnson NW, Warnakulasuriya KAAS. Evaluation of inter-incisor distance as an objective criterion of the severity of oral Submucous Fibrosis in Karachi, Pakistan. Eur J Cancer Part B Oral Oncol 1996;32:362–4. https://doi.org/10.1016/0964-1955(96)00009-7.

35. George A, Bs S, Sunil S, Varghese SS, Thomas J, Gopakumar D, et al. George A, Sreenivasan BS, Sunil S, Varghese SS, Thomas J, Gopakumar D, Mani V. POTENTIALLY MALIGNANT DISORDERS OF ORAL CAVITY. Oral & Maxillofacial Pathology Journal. 2011 Jan 1;2(1). Textb Oral Maxillofac Surg 2011.

36. Bailoor DN, Nagesh K. Fundamentals of Oral Medicine & Radiology. 2005. https://doi.org/10.5005/jp/books/10318.

37. Rose, Balan A. Oral Submucous Fibrosis - A changing scenario. J Indian Acad Oral Med Radiol 2020;19:334.

38. Kiran Kumar K, Saraswathi TR, Ranganathan K, Uma Devi M, Elizabeth J. Oral submucous fibrosis: A clinico-histopathological study in Chennai. Indian J Dent Res 2007. https://doi.org/10.4103/0970-9290.33785.

39. Koneru A, Hunasgi S, Hallikeri K, Surekha R, Shreekanth Nellithady G, Vanishree M. A systematic review of various treatment modalities for oral submucous fibrosis. J Adv Clin Res Insights 2014. https://doi.org/10.15713/ins.jcri.18.

40. Elangovan KS, Ravi SR, Sarkar VR. Autologous Bone Marrow Concentrate (Mononuclear Stem Cell) Therapy in the Treatment of Oral Submucous Fibrosis. J Indian Aca Oral Med Radiol n.d.;25:1–4. https://doi.org/10.5005/jp-journals-10011-1329.

41. Gupta D, Sharma SC. Oral submucous fibrosis-A new treatment regimen. J Oral Maxillofac Surg 1988;46:830–3. https://doi.org/10.1016/0278-2391(88)90043-2.

42. Haque MF, Meghji S, Nazir R, Harris M. Interferon gamma (IFN-γ) may reverse oral submucous fibrosis. J Oral Pathol Med 2001;30:12–21. https://doi.org/10.1034/j.1600-0714.2001.300103.x.

43. Sudarshan R, Annigeri RG, Vijayabala SS. Aloe vera in the treatment for oral submucous fibrosis - a preliminary study. J Oral Pathol Med 2012;41:755–61. https://doi.org/10.1111/j.1600-0714.2012.01168.x.

44. DESA J V. Submucous fibrosis of the palate and cheek. Ann Otol Rhinol Laryngol 1957;66:1143–59. https://doi.org/10.1177/000348945706600420.

45. Lai DR, Chen HR, Lin LM, Huang YL, Tsai CC, Lai D -R. Clinical evaluation of different treatment methods for oral submucous fibrosis. A 10-year experience with 150 cases. J Oral Pathol Med 1995;24:402–6. https://doi.org/10.1111/j.1600-0714.1995.tb01209.x.

46. Niaz K, Maqbool F, Khan F, Bahadar H, Ismail Hassan F, Abdollahi M. Smokeless tobacco (paan and gutkha) consumption, prevalence, and contribution to oral cancer. Epidemiol Health 2017. https://doi.org/10.4178/epih.e2017009.

47. Maggini S, Pierre A, Calder PC. Immune function and micronutrient requirements change over the life course. Nutrients 2018. https://doi.org/10.3390/nu10101531.

48. Forester SC, Lambert JD. Antioxidant effects of green tea. Mol Nutr Food Res 2011.

49. Karthik H, Nair P, Gharote HP, Agarwal K, Ramamurthy Bhat G, Kalyanpur Rajaram D. Role of

hemoglobin and serum iron in oral submucous fibrosis: A clinical study. Sci World J 2012. https://doi.org/10.1100/2012/254013.

50. Tai YS, Liu BY, Wang JT, Sun A, Kwan HW, Chiang CP. Oral administration of milk from cows immunized with human intestinal bacteria leads to significant improvements of symptoms and signs in patients with oral submucous fibrosis. J Oral Pathol Med 2001. https://doi.org/10.1034/j.1600-0714.2001.301007.x.

51. Yasir M, Sonthalia S. Corticosteroid Adverse Effects. 2019.

52. James L, Shetty A, Rishi D, Abraham M. Management of Oral Submucous Fibrosis with Injection of Hyaluronidase and Dexamethasone in Grade III Oral Submucous Fibrosis: A Retrospective Study. J Int Oral Heal JIOH 2015.

53. Kakar PK, Puri RK, Venkatachalam VP. Oral submucous fibrosis—treatment with hyalase. J Laryngol Otol 1985. https://doi.org/10.1017/S0022215100096286.

54. Alshadwi A, Bhatia I. Excision of Oral Submucous Fibrosis and Reconstruction with Full Thickness Skin Graft: A Case Study and Review of the Literature. Case Rep Dent 2012. https://doi.org/10.1155/2012/628301.

55. Johar N, Chaurasia S, Phulambrikar 3 1 Lecturer T, Student PG. Management of oral submucous fibrosis: A Review. Int J Oral Heal Dent n.d.;3:154–7. https://doi.org/10.18231/2395-499X.2017.0033.

56. Rai B, Kaur J, Jacobs R, Singh J. Possible action mechanism for curcumin in pre-cancerous lesions based on serum and salivary markers of oxidative stress. J Oral Sci 2010;52:251–6. https://doi.org/10.2334/josnusd.52.251.

57. Lee W-H, Loo C-Y, Bebawy M, Luk F, Mason R, Rohanizadeh R. Curcumin and its Derivatives: Their Application in Neuropharmacology and Neuroscience in the 21st Century. Curr Neuropharmacol 2013. https://doi.org/10.2174/1570159x11311040002.

58. Alok A, Singh ID, Singh S, Kishore M, Jha PC. Curcumin – Pharmacological actions and its role in oral submucous fibrosis: A review. J Clin Diagnostic Res 2015. https://doi.org/10.7860/JCDR/2015/13857.6552.

59. Chen A, Zheng S. Curcumin inhibits connective tissue growth factor gene expression in activated hepatic stellate cells in vitro by blocking NF-κB and ERK signalling. Br J Pharmacol 2008. https://doi.org/10.1038/sj.bjp.0707542.

60. Agarwal N, Prasad R, Singh D, Sinha A, Srivastava S, Singh G. Evaluation of efficacy of turmeric in management of oral submucous fibrosis. J Indian Acad Oral Med Radiol 2014;26:260. https://doi.org/10.4103/0972-1363.144998.

61. Das A D, Balan A, KT S. Comparative Study of the Efficacy of Curcumin and Turmeric Oil as Chemopreventive Agents in Oral Submucous Fibrosis: A Clinical and Histopathological Evaluation. J Indian Acad Oral Med Radiol 2010;22:88–92. https://doi.org/10.5005/jp-journals-10011-1021.

62. Yadav M, Aravinda K, Saxena VS, Srinivas K, Ratnakar P, Gupta J, et al. Comparison of curcumin with intralesional steroid injections in Oral Submucous Fibrosis - A randomized, open-label interventional study. J Oral Biol Craniofacial Res 2014;4:169–73. https://doi.org/10.1016/j.jobcr.2014.11.003.

63. Rajendran R, Rani V, Shaikh S. Pentoxifylline therapy: A new adjunct in the treatment of oral submucous fibrosis. Indian J Dent Res 2006. https://doi.org/10.4103/0970-9290.29865.

64. Soh CL, Muthusekhar MR. Treatment of Oral Submucous Fibrosis Using Split Skin Graft and a Polyethylene Stent: A Prospective Study. J Maxillofac Oral Surg 2015. https://doi.org/10.1007/s12663-014-0661-5.

65. Mokal NJ, Raje RS, Ranade S V., Prasad JSR, Thatte RL. Release of oral submucous fibrosis and reconstruction using superficial temporal fascia flap and split skin graft - A new technique. Br J Plast Surg 2005. https://doi.org/10.1016/j.bjps.2005.04.048.

66. Qayyum MU, Janjua OS, Ul Haq E, Zahra R. Nasolabial and extended nasolabial flaps for reconstruction in oral submucous fibrosis. J Korean Assoc Oral Maxillofac Surg 2018. https://doi.org/10.5125/jkaoms.2018.44.4.191.

67. Ramanujam S, Venkatachalam S, Subramaniyan M, Subramaniyan D. Platysma myocutaneous flap for reconstruction of intraoral defects following excision of oral sub mucous fibrosis: A report of 10 cases. J Pharm Bioallied Sci 2015. https://doi.org/10.4103/0975-7406.163485.

68. Kamath V V. Surgical Interventions in Oral Submucous Fibrosis: A Systematic Analysis of the Literature. J Maxillofac Oral Surg 2015. https://doi.org/10.1007/s12663-014-0639-3.

69. Angadi P V., Rao S. Management of oral submucous fibrosis: An overview. Oral Maxillofac Surg 2010. https://doi.org/10.1007/s10006-010-0209-x.

70. Fry R, Goyal S. (PDF) An approach to management of oral submucous fibrosis: current status and review of litrature. Int J Curr Res 2014;6:10598–604.

71. Chaudhary Z, Tandon S, Verma M. Treatment of oral submucous fibrosis with ErCr: YSGG laser. Indian J Dent Res 2011;22:472. https://doi.org/10.4103/0970-9290.87073.

72. Singh L, Bharathi SS, Sudhapalli S, Chopra D, Srivastava V. Management of a Patient with Oral Submucous Fibrosis Having Restricted Mouth Opening: A Case Report. 2011.

73. Patil S, Sarode SC, Sarode GS, Bhandi S, Awan KH, Ferrari M. Prosthetic rehabilitation of oral submucous fibrosis patients: A systematic review of published case reports and case series. PLoS One 2017;12. https://doi.org/10.1371/journal.pone.0184041.

74. Malik P. (PDF) Restricted Mouth Opening - Impressions making. Sch J Dent Sci 2015;2:24–9.

75. Wahle JJ, Gardner LK, Fiebiger M. The mandibular swing-lock complete denture for patients with microstomia. J Prosthet Dent 1992. https://doi.org/10.1016/0022-3913(92)90423-8.

76. Patil PG, Parkhedkar RD. New Graft-Stabilizing Clip as a Treatment Adjunct for Oral Submucous Fibrosis. J Prosthet Dent 2009. https://doi.org/10.1016/S0022-3913(09)60146-3.

77. Vastani A, Maria A, Chourasia N, Gupta A. A simple postoperative oral physiotherapy aid for edentulous patients with oral submucous fibrosis. Plast Aesthetic Res 2015. https://doi.org/10.4103/2347-9264.165447.

78. Commander SJ, Chamata E, Cox J, Dickey RM, Lee EI. Update on Postsurgical Scar Management. Semin Plast Surg 2016. https://doi.org/10.1055/s-0036-1584824.

79. Carswell L, Borger J. Hypertrophic Scarring Keloids. 2019.