A systematic review of various treatment modalities for oral submucous fibrosis

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Abstract
Oral submucous fibrosis (OSMF) is a persistent, progressive, pre-cancerous condition of the oral mucosa, which is related with betel quid chewing habit. OSMF is strongly connected with the risk of oral cancer. Studies suggest that the dysplasia is seen in about 25% of biopsied OSMF cases. Hence, it is very important to treat and manage OSMF in early stages. The purpose of this review was to highlight various treatment modalities for OSMF with little emphasis on clinical and histopathological features of OSMF. The literature was searched using “PubMed” and electronic databases from 1994 to 2013. Key words such as OSMF and treatment, treatment modalities for OSMF and management of OSMF were used. A total of 80 articles were retrieved from 1994 to 2014. Among the retrieved articles, only 20 articles were related to medical treatment procedures and four articles reviewed the entire management of OSMF. 10 papers discussed the surgical interventions and the remaining dealt with etiopathogenesis and prevalence of the OSMF. Various types of treatment modalities include conservative methods, medical management, and invasive methods like surgical elimination of the fibrotic bands and combined therapy. Our review of the literature for treatment of OSMF yielded a spectrum of treatment modalities to manage OSMF. Recent literature proves that the combination of drugs produce effective results in the management of OSMF. However, a more extensive clinical trial is necessary to come to a final conclusion about a particular treatment modality in managing OSMF.

Keywords
Conservative, combined therapy, medical, oral submucous fibrosis, surgical treatment

Introduction
Oral submucous fibrosis (OSMF) is a persistent, progressive, pre-cancerous condition of the oral mucosa, which is related with betel quid chewing habit extensively widespread in Southeast Asia and in China. OSMF was defined as an “insidious, chronic disease affecting any part of the oral cavity and sometimes the pharynx and esophagus, characterized by a mucosal rigidity of varying intensity due to the fibro-elastic changes of the juxta-epithelial layer, resulting in a progressive inability to open the mouth.”[1]

Numerous factors such as chili consumption, nutritional deficiency states, areca nut chewing, hereditary susceptibility, autoimmunity and collagen disorders have been suggested to be concerned in the pathogenesis of this condition. It is in general accepted at present that areca nut quid plays a principal role in the etiology of OSMF.[2] The copper content of areca nut is elevated, and the levels of soluble copper in saliva may go up in areca quid chewers. The enzyme lysyl oxidase is found to be unregulated in OSMF. This is a copper reliant enzyme, which plays a key role in surplus collagen synthesis and its cross-linkage leading to OSMF.[3]

OSMF is mainly seen in India, Bangladesh, Sri Lanka, Pakistan, Taiwan, and China, with a reported frequency ranging up to 0.4% in Indian rural population.[4] In recent years marked increase in the rate of OSMF is observed in many parts of India like Bihar, Maharashtra, Gujarat and Madhya Pradesh. The younger generations are suffering more due to the advent of more and more commercially freeze-dried areca-nut products in different multicolored eye-catching pouches like gutkha and pan masala.[2]
The purpose of this review was to highlight various treatment modalities for OSMF that have been published during the year 1994-2014 and little emphasis on clinical, histopathological features of OSMF.

Methods

Literature search strategy

The objective of this paper was to review the literature regarding various treatment modalities for OSMF. A literature search was conducted in March 2014. The literature was searched using “PubMed” and electronic databases such as “Google Search” from 1994 to 2014. The following key words were used:

1. OSMF and treatment
2. Treatment modalities for OSMF
3. OSMF and treatment
4. Management of OSMF.

The search was restricted to English language literature. Titles and abstracts of appropriate studies were chosen. Afterwards, the complete texts of these studies were evaluated whether they are corresponding to our inclusion criteria. The first pool of primary studies and review articles were searched for references leading to additional papers missed in the computerized searches.

Inclusion criteria

Studies were then categorized by study type, including randomized controlled studies, observational studies, or case series reports. To meet the criteria for randomized controlled studies, the study should consist of a control group and subjects that were randomly assigned to the control and interventional groups. Remaining studies included non-randomized prospective study, retrospective studies comparing two or more dissimilar interventions, or observational studies. Types of interventions included habit intervention, surgical procedures, medical treatments (i.e., systemic, sub-mucosal injection or topical agents, or physical therapy). Review articles of treatment modalities for OSMF were also included in the study.

Exclusion criteria

Studies those which were not correlated to the study purpose were expelled.

Results

The search words “Treatment modalities for OSMF” retrieved 15 relevant papers while the search words “OSMF and treatment” and “Management of OSMF” retrieved 80 articles from 1994 to 2014. Among the retrieved articles, only 20 articles were related to medical treatment procedures and four articles reviewed the entire management of OSMF. 10 papers discussed the surgical interventions and the left over dealt with etio-pathogenesis and occurrence of the OSMF [Table 1 and Figure 1].

Discussion

OSMF is one of the collagen metabolic disorders. A number of possible mechanisms have been recommended in the pathogenesis of OSMF. It is believed to involve juxta-epithelial inflammatory response and fibrosis in the lamina propria, possibly due to increased cross-linking of collagen by up-regulation of lysyl oxidase activity.

This fibrosis, or the upsurge of collagen, results from the property of areca nut, which increases collagen assembly and also decreases collagen deprivation.\(^5\)

Clinical features

Angadi et al. reported that patients particularly by means of habits with duration of 2-5 years were extra prone to develop OSMF. Highest occurrence of habits were in the range of 5-6 times/day (42.5%) while many patients also had a frequency >10 times/day. Posterior one-third of the oral cavity (buccal mucosa, retromolar area and soft palate) was mostly affected.\(^6\)

The episode between initiation of the chewing habit and the advance of clinical symptoms of OSMF varies enormously, ranging from a few months to several decades depending on the

Figure 1: Selection criteria as adopted in selecting the studies
Treatment modalities for OSMF

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kind of areca nut consumed, duration and practice of the habit. The most common early symptoms and signs are a burning sensation, blanching oral mucosa, ulceration and xerostomia. Later, the oral mucosa becomes stiff and opaque, by means of fibrous bands on the buccal mucosa [Figure 2], soft palate, lips, and tongue causing limit in mouth opening, intricacy in mastication, speech and swallowing.\(^7\)

Progress of fibrous bands in the lip makes the lip bulky, tough and hard to retract or evert [Figure 3]. Depapillation tongue in the tip and lateral margins may take place with blanching or fibrosis of the ventral mucosa [Figure 4]. Soft palate may be widely blanched, and uvula is shrunken in 17% of cases appearing as a small bud or hockey stick [Figure 5].\(^7,8\)

**Histopathological features**

The majority of the cases demonstrate epithelial atrophy with loss of rete ridges, epithelial atypia, and pigment incontinence. Lamina propria shows widespread fibrosis of collagen fibers with a chronic inflammatory cell infiltrate [Figure 6]. In later stages, subepithelial hyalinization with atrophic changes in minor salivary glands and skeletal muscle can also be seen.

**Table 1:** The documented studies for each treatment modality

<table>
<thead>
<tr>
<th>Treatment modality</th>
<th>Group</th>
<th>Studies done</th>
</tr>
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<tbody>
<tr>
<td>Conservative treatment</td>
<td>Restriction of habits/behavioral therapy</td>
<td>Murti et al., 1990, Avon et al., 2004</td>
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<td></td>
<td>Nutritional or Supportive therapy</td>
<td>Kumar et al., 2007, Zaveri et al., 2006, Tai et al., 2001</td>
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<td></td>
<td>Oral physiotherapy</td>
<td>Cox and Zoellner, 2009</td>
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<td></td>
<td>Microwave diathermy</td>
<td>Gupta et al., 1980</td>
</tr>
<tr>
<td>Medical treatment</td>
<td>Steroids</td>
<td>Jayavel et al., 2012</td>
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<tr>
<td></td>
<td>Hyaluronidase</td>
<td>Kakar et al., 1985</td>
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<tr>
<td></td>
<td>Collagenase</td>
<td>Lin and Lin, 2007</td>
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<td></td>
<td>Placental extracts</td>
<td>Sur et al., 2003, Katharia et al., 1992</td>
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<td></td>
<td>Chymotrypsin</td>
<td>Gupta and Sharma, 1988</td>
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<td></td>
<td>INF-gamma</td>
<td>Haque et al., 2001</td>
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<td></td>
<td>Aloe vera</td>
<td>Silvia et al., 2008, Sudarshan et al., 2012</td>
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<td></td>
<td>Turmeric</td>
<td>Rai et al., 2010</td>
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<td></td>
<td>Pentoxifylline therapy</td>
<td>Rajendran et al., 2006</td>
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<tr>
<td>Surgical treatment</td>
<td>Nasolabial flaps and lingual pedicle flaps</td>
<td>Khanna and Andrade, 1995</td>
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<tr>
<td></td>
<td>The use of buccal fat pad as a grafting source</td>
<td>Saravanan and Narayanan, 2012</td>
</tr>
<tr>
<td></td>
<td>ErCr: YSGG lasers</td>
<td>Chaudhary et al., 2011, Anil et al., 2005</td>
</tr>
<tr>
<td>Combined therapy</td>
<td>Combination of steroids and topical hyaluronidase</td>
<td>Vasant et al., 2012</td>
</tr>
<tr>
<td></td>
<td>Nutritional and iron supplements with intralesional injection therapy using hyaluronidase, dexamethasone and topical application of triamcinolone acetonide 0.1%</td>
<td>Kumar et al., 2011</td>
</tr>
</tbody>
</table>

INF: Interferon, ErCr: YSGG: Erbium chromium yttrium scandium gallium garnet

Figure 2: Intraoral photograph of the buccal mucosa showing blanched oral mucosa with pigmentation

OSMF does not revert spontaneously or on termination of areca nut chewing. Once the disease is evident, it either persists or becomes more severe with contribution of additional areas of the oral mucosa. OSMF is strongly connected with the risk of oral cancer. Studies suggest that dysplasia is seen in relation to
Figure 3: Intraoral photograph showing extensive blanching and fibrosis of lower labial mucosa

Figure 4: Intraoral photograph showing depapillation on the dorsal surface of the tongue

Figure 5: Intraoral photograph showing blanched soft palate and deformed uvula shrunken into bud shape

Figure 6: Oral submucous fibrosis showing atrophic epithelium with chronic inflammation and dense fibrosis in the submucosa with degenerating muscle fibers (H and E, × 100)

25% of biopsied OSMF cases. Hence, it is very significant to treat and manage OSMF in early stages.

Treatment modalities

In current years many researchers have elicited and worked upon, the existing etiology/pathophysiology concerned to OSMF. Until date, no efficient treatment is accessible for this progressively disabling condition with elevated malignant potential. Management of OSMF thus postulates major challenge for an oral physician/oral surgeon.

Various types of treatment modalities include conservative methods, medical management, and invasive methods like surgical elimination of the fibrotic bands and combined therapy.

Conservative treatment can be categorized into restriction of habits/behavioral therapy, nutritional or supportive therapy and oral physiotherapy.
Restriction of habits/behavioral therapy

The consumption of chilies, pan, betel nut, spices and commercially available, guthka, pan masala, is ever-increasing in India. Accordingly people should be encouraged to stop these habits so as to prevent OSMF. Affected patients should be explained about the disease and possible malignant potential of OSMF. Possible irritants should be removed. Those patients with this incurable, persistent fibro-elastic scarring disease necessitate being fully motivated. Motivation is essential at least in the early stages, as it could possibly slow the progress of the disease.\[5\]

An intervention study has shown a decline in the risk for OSMF as a consequence of education against chewing habits. There was a drop in the incidence of OSMF from 21.3/100,000 persons among men in the control cohort to 8.3 in the intervention cohort, and from 45.7 to 29.0 among women in the control cohort. This reduction in the percentage highlighted the decreased risk with the decline in areca nut habit.\[10\] Avon et al.\[11\] also reported improvement in mucosal lesion as well as clinical symptoms subsequent to the cessation of the areca nut chewing habit.

Nutritional or supportive therapy

Micronutrients and minerals such as vitamin A, B, C, D and E, iron, copper, calcium, zinc, magnesium, and selenium can efficiently diminish the oxidant levels. A low ingestion of fruits and vegetables is linked with an increased risk for pre-cancers and cancers.\[12\]

Ingestion of red tomatoes, green leafy vegetables and fresh fruits should be included in the regular diet since these deliver protection against the increased risk of cancer by rising levels of antioxidants.\[8,9\] Lycopene is a carotenoid present in tomatoes has been revealed to have a number of effective antioxidant and anti-carcinogenic properties and has established intense benefits in precancerous lesions for instance leukoplakia. Lycopene has been shown to reduce hepatic fibrogenesis and may exert a similar inhibition on abnormal fibroblasts in OSMF.\[13\]

Intake of green tea should be incorporated in the diet chart. Polyphenols in green tea have considerable free radical scavenging activity and can protect cells from DNA damage caused by reactive oxygen species. It can also hinder tumor cell proliferation and induce apoptosis. Tea catechins have been shown to reduce angiogenesis and tumor cell invasiveness. Furthermore, green teas have been shown to activate detoxification enzyme, such as glutathione S-transferase which may help defend next to tumor development. Thus, many of the potential beneficial special effects of tea have been ascribed to the strong antioxidant activity of tea polyphenols.\[14\]

Various studies have concerned the deficiency of iron both as a cause and consequence in etio-pathogenesis of OSMF. Thus, routine assessment of hemoglobin levels followed by iron supplements should be incorporated in the treatment plan.\[8,9\]

Immune milk is a variety of skimmed milk formed from cows immunized with several human intestinal bacteria. It has 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. Chemically it is alike to commercial milk however it contains 20-30% elevated concentration of IgG Type I antibody. Tai et al. showed that oral supervision of milk from cows immunized with human intestinal bacteria lead to a substantial improvement in signs and symptoms of patients with OSMF. Presence of IgG antibody in immunized milk might restrain the inflammatory reaction and modulate cytokine assemblage in OSMF patients which is foremost to significant improvement.\[15\]

Oral physiotherapy

Physiotherapy can transform tissue remodeling during promotion of physical movements within physiological limits producing noteworthy results. Physiotherapy in OSMF can be in the form of physical exercise regimen and splints or other devices. Muscle stretching exercises intended for the mouth may be supportive to avoid further limitation of mouth movements. This includes forceful mouth opening with the assist of sticks, hot water gargling and ballooning of mouth. This is considered to put pressure on fibrous bands. Forceful mouth opening have been tried with mouth gag and acrylic surgical screw.\[19\]

Cox and Zoellner advocated 5 times every day for physiotherapy by inter-positioning tongue spatulas stuck between teeth and addition of a new spatula every 5-10 days for 4 months. It was observed that oral opening was enhanced in OSMF patients.\[16\]

Microwave diathermy

Heat has been adequately used in the form of hot rinses, lukewarm water or selective deep heating therapies like shortwave and microwave diathermy. Heat therapy acts by fibrinolysis of bands. Short-wave produces sharp localized deep heat, avoids the unintentional heating of superficial facial tissues like skin and adipose tissue. Microwave diathermy selectively heats only juxta-epithelial connective tissue and limiting the area to be treated. Thus, it is easy to apply with minimum discomfort.\[9,11\]

Gupta et al. advocated diathermy every day for 20 min at each site of lesion by means of 20-25 watts of energy to create comfortable warmth. Such 15 sittings were given to each patient and found helpful for the moderately advanced stage of OSMF.\[17\]

Medical treatment

Treatment includes intralesional injection of steroids, placentrex and fibrinolytic agents. Medical treatment is symptomatic and intended at improving movements.

Steroids

Steroids are well recognized to act as immunosuppressive agents causing inhibition of inflammation found in OSMF lesions, thus reducing this fibro-collagenous condition. In addition, steroids can slow down the proliferation of fibroblasts and thus reducing the number of collagen fibers. Steroids can also liberate cellular proteases in the connective tissue, which in turn can activate the collagenase and zymogen that consume insoluble collagen.\[1,12,18\]
Submucosal intralesional injections weekly or topical application of steroids in patients with moderate OSMF may help to avoid additional damage. Steroid ointment applied topically may be helpful in ulcers and painful oral mucosa. A local injection of hydrocortisone 1.5 cc is found to be efficient.\(^{[12]}\)

**Hyaluronidase**

*In vitro* studies, hyaluronidase attacks quickly on collagen from OSMF patients than on normal collagen. Hyaluronidase degrades the hyaluronic acid matrix, lowers the thickness of intracellular cemental substances as well as activating definite plasmatic mechanisms. As a result, reprise of trismus may be predictable through softening and diminishing of fibrous tissue.\(^{[1]}\)

The use of topical hyaluronidase has been revealed to improve symptoms more quickly than steroids only. Hyaluronidase can also be supplementary to intra-lesional steroid preparations. The mixture of steroids and hyaluronidase showed improved long-term results. 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.\(^{[19]}\)

**Collagenase**

An endogenous collagenase action in normal oral mucosa exhibits 3 to 5 fold higher levels than that of OSMF tissues. Reduced content of functional collagenase observed in OSMF patients is one of the mechanisms accountable for collagen accumulation. Lin and Lin found that intra-lesional collagenase injections not only results in a noteworthy improvement of mouth opening, but also experience a striking decline in hypersensitivity to spices, cold, and heat which helps to re-establish eating function.\(^{[9,20]}\)

**Placental extracts**

The injection placentrex is an aqueous extort of human placenta containing nucleotides, enzymes, aminoacids, steroids and vitamins. It acts by “biogenic stimulation”. Its use is mainly due to the method of “tissue therapy” introduced by Filatov in 1933 and later in 1953. His theory states, “animal and vegetable tissues, when detached from the parent body and exposed to conditions unfavorable, but not mortal to their existence, undergo biological readjustment leading to the development of substances in condition of their survival to ensure their vitality. Such tissues or their extracts, implanted or injected into the body after conflict to pathogenic factors, stimulate the metabolic or regenerative processes, thereby favoring recovery.\(^{[9]}\)

The aqueous extract of placenta acts as follows:

1. Hasten cellular metabolism
2. Aids in the assimilation of exudates
3. Stimulates regenerative development
4. Increases physiological purpose of organs
5. Produces noteworthy enhancement of wound healing
6. Has an anti-inflammatory consequence.\(^{[9]}\)
7. Sur and Bis was showed that it is a necessary biogenic stimulator. It stimulates pituitary adrenal cortex and regulates metabolism of tissue. It also increases vascularity of tissue.\(^{[21]}\)

Katharia et al. carried out a study on 22 OSMF patients and injection of 2 ml placental extract (Inj. placentrex) was given locally in the preset areas, once a week up to a total duration of one mouth. The results showed that the severity of the disease was reduced.\(^{[21]}\)

**Chymotrypsin**

Chymotrypsin is an endopeptidase enzyme that can execute proteolysis. Chymotrypsin preferentially cleaves peptide amide bonds where the carboxyl side of the amide bond is a tyrosine, tryptophan, or phenylalanine of collagen fibers in OSMF. Chymotrypsin, thus acts as a proteolytic agent in the treatment of OSMF. Gupta and Sharma injected Chymotrypsin (5000 IU), dexamethasone (4 mg) and hyaluronidase (1500 IU) twice weekly for 10 weeks sub-mucosally in OSMF patients and observed good results.\(^{[8,23]}\)

**Interferon (IFN)-gamma**

IFN-gamma plays a significant role in the treatment of OSMF for the reason that it has immuno-regulatory effect. Haque et al. studied that IFN-gamma is a known antifibrotic cytokine, effect of which was considered on collagen synthesis by arecoline stimulated OSMF fibroblast. Results of this study showed that there was inhibition of collagen synthesis in existence of IFN-gamma. This clinical trial of IFN-gamma intra-lesional injections gave major progress in mouth opening.\(^{[24]}\)

**Aloe vera**

* A. vera, popularly known as “babosa,” is a plant usually found the Northeast of Brazil. Its foliage, extract and resin present antimicrobial, anti-inflammatory and healing properties and are indicated to hepatic and stomach diseases.\(^{[23]}\)

Sudarshan et al. has carried out a preliminary study to contrast the efficacy of *A. vera* with antioxidants in the treatment for OSMF. Results of this study showed that *A. vera* response is enhanced in all the parameters evaluated and responded in all the clinico-histopathological stages chiefly in patients with mild-stage clinically and early-stage histopathologically. *A. vera* as well showed 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 thus enhances the patients’ fulfillment.\(^{[26]}\)

**Turmeric**

Curcumin (diferuloylmethane) found in turmeric, a natural yellow pigment exhibits anti-oxidant, anti-inflammatory and anti-cancer properties. Turmeric oil and turmeric oleoresin together offers defense against DNA damage. As such, it may fulfill two roles in the putative treatment of OSMF, both as an anti-inflammatory agent and as a chemopreventive agent. It also provides a base for a simple, safe, acceptable and cost effective interference for earlier stages of OSMF.\(^{[25]}\) Rai et al. conducted a study using curcumin in the treatment of oral precancers including 25 patients with OSMF. This study reported that OSMF was “cured by curcumin” due to increasing of local and systemic antioxidative status.\(^{[27]}\)
Pentoxifylline therapy

Pentoxifylline is a methylxanthine derivative that produces dose-related hemorrheologic effects. It can act in these possible ways:
1. Microcirculation is progressed and platelet aggregation as well as granulocyte adhesion is reduced
2. Leukocyte deformability is amplified and as well as slows down neutrophil adhesion and activation
3. Has antithrombin, antiplasmin, and fibrinolytic activity
4. It can cause degranulation of neutrophils, increases natural killer cell activity and inhibits T-cell and B-cell activation
5. It can maintain cellular integrity and homeostasis following acute injury
6. Pentoxifylline reduces burn scar contractures
7. This drug can also reduce the symptoms in patients with OSMF, in addition to its function in improving the vascularity.\[28\]

Rajendren et al. used pentoxifylline as an accessory drug in OSMF treatment and after 7 months trial and 6-12 months follow-up, the patients showed progress in signs and symptoms as compared to controls.\[28\]

Surgery

It is the technique of choice in patients with limited mouth opening and/or biopsy showing dysplastic or neoplastic changes.\[7,8\]

The following surgical modalities have been used:
- Simple excision of the fibrous bands can be done. However, this excision can result in contracture of the tissue and exacerbation of the condition
- Split-thickness skin grafting following bilateral temporalis myotomy or coronoidectomy. Trismus associated with OSMF possibly due to changes in the temporalis tendon secondary to OSMF; therefore, skin grafts may relieve symptoms
- Nasolabial flaps and lingual pedicle flaps can be performed. Surgery to create flaps is executed only in patients with OSMF in whom the tongue is not involved.\[29\]
- Buccal fat pad is used as a grafting source. The buccal fat pad is a flexible and lobulated mass, simply accessible, and mobilized. Mehrotra et al. compared the surgical treatment modalities in 100 patients using buccal fat pad, tongue flap, nasolabial flap, and split thickness graft and concluded that buccal fat pad graft was superior to all the other surgical procedures, and that can be done even under local anesthesia as a day care procedure.\[29\]

Lasers offer oral surgeons with a new modality for treating OSMF. The erbium chromium yttrium scandium garnet (ErCr:YSGG) laser has a wavelength of 2780 nm, well absorbed by water and is used on oral soft tissue without creating thermal damage. The overall advantage of laser surgery include a somewhat bloodless operative field and thus outstanding visibility, reduced need for local anesthesia, the less probability of bacterial infection, reduced mechanical tissue trauma, fewer sutures, quicker healing, reduced post-operative edema, scarring and tissue shrinkage. Chaudhary et al., highlights the attempt in treating a moderate case of bilateral OSMF with ErCr:YSGG laser showed a better end result during follow-up.\[31,32\]

Advantages of using lasers in treating OSMF were the charred tissue obtained after excision of bands provided a protective environment for the incised raw areas until the initial healing took place, resulting in less scar-tissue formation. Shah et al. reported that the ultimate outcome of using lasers in OSMF was excellent. The average increase of mouth opening was 15.0 mm in moderately advanced cases and 17.0 mm in early cases over a follow-up period of 3 months. Less scar formation led to more flexible and elastic mucosa. Due to this there was no recurrence or tissue shrinkage after surgery, maintaining good mouth opening.\[32\]

Combined therapy

With the combination of peripheral vasodilators (nylidrin hydrochloride), vitamin D, E and B complex, placental extract, local and systemic corticosteroids and physiotherapy claim a high success rate in OSMF management. The grouping of steroids and topical hyaluronidase shows enhanced long-term results than used alone.\[8,33\] Kumar et al. reported that combined therapy employing nutritional and iron supplements with intra-lesional injection therapy using hyaluronidase, dexamethasone and placenxtrix in addition to local anesthetic topical gel and topical application of triamcinolone acetonide 0.1% caused a marked improvement in patients signs and symptoms. Evidenced by improvement in color of the oral mucosa, decrease in blanching and decreased severity of burning sensation, increased mouth opening and tongue

<table>
<thead>
<tr>
<th>Clinical staging</th>
<th>Treatment Modalities</th>
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<tr>
<td>Grade I</td>
<td>1. Presence of only blanching of oral mucosa without symptoms.</td>
</tr>
<tr>
<td>Grade II</td>
<td>1. Grade I and 2. Presence of blanching, burning sensation, dryness of the mouth and vesicles or ulcers in the mouth.</td>
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<tr>
<td>Grade III</td>
<td>1. Grade II and 2. Restriction of mouth opening with palpable bands all over the mouth without tongue involvement.</td>
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<tr>
<td>Grade IV</td>
<td>1. Grade III and 2. Tongue involvement.</td>
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<tr>
<td>Grade V</td>
<td>1. Grade IV 2. Chronic ulcer and histopathologically proven Carcinoma.</td>
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</table>

Figure 7: Various treatment modalities given in combination at different stages of oral submucous fibrosis
protrusion. However, in most of the cases, depending on the stage of disease and extent of oral involvement, surgery consisting of a combination of drugs is preferred in cases with minimal impairment of mouth opening and surgery might be useful in patients with marked limitation of mouth opening [Figure 7].

Conclusion

Our review of the literature for treatment of OSMF yielded a spectrum of treatment modalities to manage OSMF. Numerous treatment modalities that have been implicated to cure the disease are the use of corticosteroids, hyaluronidase, placenix, IFN, and microwave diathermy, etc. Surgical treatment is also considered by excision of fibrotic tissues and covering the defect with grafts. Though, till date, there is no single method which can be used as the definitive treatment modality for OSMF. Recent literature proves that the combination of drugs produce effective results in the management of this disease. A more extensive clinical trials involving a greater number of cases and including more parameters are necessary to come to a final conclusion about a particular modality in the management of OSMF.

References