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THERAPEUTIC APPROACHES FOR ORAL SUBMUCOUS FIBROSIS: SUPPORTIVE CARE STRATEGIES

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ABSTRACT
Oral Submucous Fibrosis (OSMF) is a precancerous condition affecting the oral mucosa, oropharynx, and, rarely, the larynx. It is primarily caused by habits such as areca nut chewing, pan masala chewing, smoking, and consuming hot and spicy foods like chilies. Various treatment modalities are employed to provide symptomatic relief. This article compiles published literature on adjuvant therapies for treating OSMF. The literature suggests the use of garlic, curcumin, tulsi, aloe vera, spirulina, and lycopene as treatment options for OSMF. The relevant studies indicate that these adjuvant therapies offer a natural and cost-effective treatment option. Additionally, lifestyle modifications can aid in curing the disease. However, further studies are needed to enhance awareness and encourage the use of these non-invasive therapeutic modalities as primary treatment options by patients.

KEYWORDS: OSMF, Curcumin, Aloe vera, Tulsi, Lycopene

INTRODUCTION
In 1966, Pindborg defined OSMF as “an insidious chronic disease affecting any part of the oral cavity and sometimes the pharynx. Although occasionally preceded by or associated with vesicle formation, it is always accompanied by a juxta-epithelial inflammatory reaction, followed by fibroblastic changes in the lamina propria, with epithelial atrophy leading to stiffness of the oral mucosa, causing trismus and difficulty in eating.”[1]

OSMF was first reported in India in 1953 by Joshi, who coined the term "submucous fibrosis of the palate and faucial pillars."[2] Various other names have been suggested, including diffuse oral submucous fibrosis, idiopathic scleroderma of the mouth, idiopathic palatal fibrosis and sclerosing stomatitis [2].

The incidence of OSMF is notably higher among South East Asians and the Indian population, with an elevated rate of incidence from the past to the present. Reports from North Western India indicate an incidence of 2.6 and 8.5 per 100,000 per year for males and females, respectively; figures from South India are higher, with 9 and 20 per 100,000 per year for males and females, respectively.[3]

Different etiologies have been proposed earlier, including chills, nutritional deficiency, autoimmunity, and genetic susceptibility [4]. Currently, the primary etiology of OSMF is associated with the use of areca nut and quid chewing habits. Areca nuts contain alkaloids, with arecoline being a primary etiologic factor. Arecoline has the ability to modulate matrix metalloproteinases, lysyl oxidases, and collagenases, which affect collagen metabolism and subsequently lead to increased fibrosis [5].

Symptoms of OSMF vary with the progression of the disease. Early signs include mucosal ulcerations, a burning sensation, and stiffness. As the disease progresses, blanching of the oral mucosa occurs. The most distinctive characteristic of OSMF is the presence of palpable fibrous bands in the oral mucosa [6], leading to marked stiffness and difficulty in opening the mouth [7]. Other symptoms include dryness of the oral cavity, recurrent ulcers, oral mucosal pigmentation, burning sensation, and reduced ability to open the mouth and protrude the tongue. Histopathological examination reveals subepithelial fibrosis and chronic inflammation, followed by hyalinization, vascular loss, parakeratosis, and squamous hyperplasia [8].

Various treatment protocols have been attempted to alleviate the signs and symptoms of OSMF. These include intralesional injections of corticosteroids, placental extracts, hyaluronidase alone or in combination, laser treatment, surgical intervention, IFN-gamma, peripheral vasodilators, minerals, sugars, lignin, immune milk, turmeric, lycopene, and micronutrient supplements. Several physiotherapeutic modalities have also shown favorable results [9]. Natural Ayurvedic treatments, along with lifestyle changes, can help to reduce the symptoms of OSMF and provide relief to patients without causing side effects [10]. This article reviews various adjuvant treatment modalities for OSMF.

ADJUVANT THERAPIES

Garlic

Plants of the Allium genus are recognized for producing organosulfur compounds with notable biological and pharmacological properties. Among these, garlic (*Allium sativum*) is one of the most commonly used. Once extracted and isolated, these compounds exhibit a broad range of beneficial effects, including antimicrobial, cardioprotective, anticancer, and anti-inflammatory activities [11]. Garlic is a natural bioactive component frequently used in Ayurvedic medicine for various diseases. The main component of garlic, allicin, is known for its anti-inflammatory properties and immunomodulation. Allicin has been found to effectively reduce inflammatory product secretion, inhibit neutrophil migration, and combat bacteria and viruses. It also interferes with oxidation and plays a crucial role in immunomodulation [12].

Curcumin

Curcumin is a polyphenolic compound isolated from the plant *Curcuma longa* (Zingiberaceae), found in Southern Asia. The medicinal properties of turmeric, which is a source of curcumin, have been extensively studied, focusing on its bioactive materials and mechanisms of action. Curcumin has three notable qualities: inhibition of lipid peroxidation,

suppression of cellular proliferation, and inhibition of collagen synthesis. Many studies have demonstrated that curcumin improves mouth opening and reduces the burning sensation in patients with OSMF. Its antioxidant activity, first reported in 1975, acts as an oxygen free radical scavenger. Curcumin also has a potent inhibitory effect on H_2O_2 induced damage in human keratinocytes and fibroblasts.

Aloe Vera

Aloe Vera possesses strong anti-inflammatory properties and acts as a wound-healing agent. Aloe Vera reported significant improvement in the burning sensation and mouth opening compared to other antioxidant treatments. Aloe Vera contains 75 potentially active constituents, including vitamins, enzymes, minerals, sugars, lignin, saponins, salicylic acids, and amino acids. Vitamins A (beta-carotene), C, and E are antioxidants that help neutralize free radicals. Bradykinase in Aloe Vera helps reduce inflammation when applied topically. The polysaccharides in Aloe Vera gel have wound healing, anti-inflammatory, anticancer, immunomodulatory, and gastroprotective properties, suggesting its potential use in managing OSMF.

Tulsi

Tulsi enhances immunity and metabolism. It has been found to inhibit enzymes that reduce inflammation and alleviate depression. Tulsi exhibits antioxidant, anti-inflammatory, chemopreventive, anticancer, and immunomodulatory properties. According to Aditi Srivastava et al., Tulsi's synergistic activity has shown significant effectiveness in OSMF therapy. In the first month of the trial, Tulsi caused a substantial reduction in the burning sensation and a significant improvement in mouth opening, both clinically and statistically. In severe cases, the findings indicated greater efficacy with Tulsi.

Spirulina

Spirulina, a blue-green algae, is rich in proteins, carotenoids, and other micronutrients. It has shown promising results in treating leukoplakia due to its chemopreventive capacity, which is attributed to its high antioxidant content, including beta-carotene and superoxide dismutase Spirulina has been effective in treating OSMF patients. Its successful management of OSMF is due to its antioxidant, anti-inflammatory, and immunomodulating properties.

Lycopene

Lycopene is a potent antioxidant derived from tomatoes and is produced through the Lyc-O-Mato process, which retains its natural proportions with other compounds in marketed pharmacological preparations. Lycopene has the highest single oxygen quenching capacity among dietary carotenoids in vitro. There is an inverse relationship between lycopene intake and the risk of various cancers, including prostate, pancreas, bladder, cervix, and oral leukoplakia, due to its ability to modulate dysplastic changes. New evidence suggests that lycopene's anticancer activity also involves the upregulation of connexin and stimulation of gap junctional communication, independent of its antioxidant role.

Turmeric

Turmeric contains curcumin, a naturally occurring yellow pigment with anti-inflammatory, anticancer, and antioxidant properties. Turmeric oil and turmeric oleoresin together protect against DNA damage. Therefore, turmeric may serve as both an anti-inflammatory agent and a chemopreventive agent in the treatment of OSMF. It offers a simple, safe, acceptable, and cost-effective intervention for the early stages of OSMF. Rai et al. conducted a study using curcumin in the treatment of oral precancers, including 25 patients with OSMF. This study reported that curcumin effectively "cured" OSMF by increasing local and systemic anti-oxidative status.

CONCLUSION

OSMF is a chronic and debilitating illness with a multifactorial etiology, and no single traditional therapy has proven conclusively effective. Adjuvant medicine is often used for extended periods due to its fewer side effects, safety, and lower cost, making it a suitable complement to traditional OSMF treatments. The literature suggests that adjuvant therapies can be effective in managing oral submucous fibrosis. However, there is insufficient evidence to establish a definitive form of treatment. Therefore, more comprehensive studies are needed to enhance the understanding and efficacy of adjuvant therapy for treating OSMF.

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