

Supportive therapy for oral submucous fibrosis

Anjum Ara Jamebaseer Farooqui

Dr Anjum Ara J Farooqui, Dr Sakina Sattar, Dr Jamebaseer M Farooqui, Dr Vikrant Kasat

Corresponding author, Associate professor in the department of Oral Medicine and Radiology. Rural Dental College, Pravara Institute of Medical Sciences, Loni.:

, Senior Lecturer in the department of Orthodontics. Rural Dental College, Pravara Institute of Medical Sciences, Loni.:

Professor in the department of Forensic Medicine and Toxicology, Dr Balasaheb vikhe patil, Rural Medical College, Pravara Institute of Medical Sciences, Loni.:

Associate Professor in the department of Oral Medicine and Radiology, Govt Dental College, Chhatrapati Sambhaji Nagar.

Date of Submission: 01-05-2024

Date of Acceptance: 10-05-2024

ABSTRACT

Oral Sub mucous Fibrosis (OSMF) is a precancerous condition including oral mucosa, oropharynx, and rarely the larynx resulting from habits like areca nut chewing, pan masala chewing, smoking and consumption of hot and spicy food like chilies. The various treatment modalities are used to provide symptomatic relief. This article is the collection of published literature on the adjuvant therapies in treating OSMF. The literature suggest the use of garlic, cur cumin, tulsi, aloe vera, spirulina, and lycopene as treatment modalities for OSMF. The relevant literature proves that these adjuvant modalities promise a natural and cost-effective treatment option along with lifestyle modification will help in curing the disease.

Though studies need to be evaluated to enhance its awareness and use by patients as a primary non invasivetherapeutic modality.

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

I. INTRODUCTION

In 1966 Pindborg defined OSMF as “an insidious chronic disease affecting any part of the oral cavity and sometimes the pharynx. However occasionally preceded by and or associated with a vesicle formation, it is always associated with 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 and he coined the term sub mucous fibrosis of palate and faucial pillars.[2] Various other names suggested were diffuse oral sub mucous fibrosis (Lal, 1953), idiopathic scleroderma of the mouth (Su, 1954), idiopathic palatal fibrosis (Rao, 1962) and sclerosing stomatitis (Behl, 1962).[2]

Incidence of OSMF disease commonly occurs in the South East Asians and Indian population. Indian population has an elevated rate of incidence from the past to the present. Reports from the North Western India give an incidence of 2.6 and 8.5 per 100,000 per year for males and females, respectively; figures in south of India were higher 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.[2] Currently, the etiology of OSMF is mainly associated to the use of areca nut and quid chewing habit.[3] Areca nuts include alkaloids, of which arecoline seems to be a primary etiologic factor. Arecoline has the ability to modulate matrix metalloproteinases, lysyl oxidases, and collagenases which affects the metabolism of collagen and subsequently leading to an increased fibrosis. [4]

Symptoms of OSMF differ with progression of disease. Early signs are ulcerations of the mucosa, feeling of burning sensation,

stiffness and blanching of oral mucosa occurs as the disease progress. The most distinctive characteristic of OSMF is palpable fibrous bands in oral mucosa[5,6] that results in marked stiffness and difficulty in mouth opening. [7, 8] Other characteristics of the disease include dryness of oral cavity, recurrent ulcer and pigmentation of the oral mucosa, burning sensation, reduced opening of the mouth and protrusion of the tongue. Histopathological review reveals sub epithelial fibrosis and chronic inflammation which is followed by hyalinization and vascular loss, parakeratosis squamous hyperplasia.[9,10]

The different treatment protocols which have been attempted to recover the signs and symptoms of OSMF comprises intralesional injections of corticosteroids, placental extracts, hyaluronidase alone or in combination, laser treatment, surgical, IFN-g , peripheral vasodilators administration, minerals, sugars, lignin, immune milk, turmeric, lycopene and micronutrient supplements. Various physiotherapeutic modalities have also shown favorable results.[11] Natural ayurvedic treatment along with lifestyle change can help to lessen the symptoms of OSMF and hence provide relief to the patient without having to cause side effects.[12]This article provides a review of various adjuvant treatment modalities of OSMF.

II. ADJUVANT THERAPIES

Garlic

Plants of the allium genus are recognized for producing oregano sulfur compounds which have interesting biological and pharmacological distinctiveness. Of these, garlic (*Allium sativum*) is among the most regularly used. Once extracted and isolated, these compounds show a broad range of favorable effects against microbial infections as well as cardio protective, anticancer and anti-inflammatory activity. [13] Garlic is a natural bioactive component regularly used in the ayurvedic medicine for a number of diseases. The main component of garlic is allicin that is considered to have anti-inflammatory properties and immunomodulation. Allicin has been founded to efficiently decrease inflammatory product secretion, migration of neutrophils, inhibit bacteria and viruses. They also interfere with oxidation and play an important role in immunomodulation. [14]

Curcumin

Curcumin is a plant isolated polyphenol (*Curcuma longa*). (Zingiberaceae) compound found in Southern Asia. The exact mechanism of action

and determination of bioactive materials have been examined for the medicinal properties of turmeric which is cur cumin source. It has three qualities such as lipid peroxidation inhibition, cellular proliferation screening and inhibition of collagen synthesis. Many studies show effects cur cumin in increased mouth opening of patient with OSMF. Studies shows improvement in mouth opening and burning sensation. Cur cumin's antioxidant activity was reported in 1975. It acts as an oxygen free radical scavenger. Cur cumin has a powerful inhibitory effect in human keratinocytes and fibroblasts against H₂O₂ induced damage. [15-19]

Aloe Vera

Aloe Vera is highly anti-inflammatory and works as a wound-healing hormone and serols. Sudarshan et al reported improvement of burning sensation and opening of the mouth compared with other antioxidant treatment. Aloe Vera constitutes 75 potentially active constituents which includes vitamins, enzymes, minerals, sugars, lignin, saponins, salicylic acids and amino acids. Vitamins are vitamin A (beta-carotene), C and E which are antioxidants and help to neutralize free radicals. Brady kinase helps decrease inflammation when applied topically to the skin or mucosa. The gel of aloe vera leaves contained polysaccharides which has wound healing, anti-inflammatory, anticancer, immuno modulatory and gastro protective properties. Properties of aloe vera suggest the possibility of its use in the management of OSMF. [20]

Tulsi

Tulsi increases immunity and enhances metabolism. It is an extract which has been found inhibiting enzymes to reduce inflammation. It is also lessens depression.[21] It has anti-oxidant, anti-inflammatory, chemo-preventive, anti-carcinogenic and immunomodulatory etc. [22] According to Aditi Srivastava et al., the synergistic activity of tulsi has resulted in greater effectiveness in OSMF therapy. During the first month of trial it caused an early, prolonged and substantial decrease in burning sensation, both clinically & statistically and amount of mouth opening has also changed significantly. In extreme cases, the findings were better represented with its greater efficacy. [23]

Spirulina

Spirulina is a blue green algae which is rich in natural source of proteins, carotenoids and other micronutrients. It has been in essence in

treating leukoplakia with promising results. The chemo preventive capacity to reverse precancerous lesions of spirulina is attributed to its antioxidant property with high amount of beta carotene and superoxide dismutase [24]. According to Shetty P et al spirulina shows effective result in treating OSMF patients. [25] Use of spirulina in the successful management of OSMF is attributed to its antioxidant, anti-inflammatory and immunomodulating properties. [25]

Lycopene

Lycopene is a powerful antioxidant obtained from tomatoes and manufactured by the Lyc-O-Mato process whereby it retains its natural proportions with other compounds in the marketed pharmacological preparations. Lycopene has the maximum single oxygen quenching capacity with other free radicals in vitro among dietary carotenoids. The contrary relationship between lycopene intake and cancer risk has been observed in particular form of cancers of prostate, pancreas, bladder, cervix, and oral leukoplakia because of its ability to modulate dysplastic changes. New evidence has provided other explanations for the anticancer activity of lycopene by the up regulation of connexin and stimulation of gap junctional communication, an action that is independent of its role as an antioxidant.[27]

Turmeric

Turmeric contains the naturally occurring yellow pigment curcumin, which has anti-inflammatory, anti-cancer, and antioxidant properties. [28] 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 chemo preventive agent. It also provides support for a simple, safe, acceptable and cost effective interference for earlier stages of OSMF. [29] Rai et al. carried out study using curcumin in the treatment of oral pre cancers including 25 patients with OSMF. This study reported that OSMF was "cured by curcumin" due to increasing of local and systemic antioxidant status. [30]

III. CONCLUSION

OSMF is a chronic debilitating illness, of multifactorial etiology and no single traditional therapy has proven conclusive. Adjuvant medicine is expected to be used for longer periods of time, because they have fewer side effects. It is said to be safe and cost is also less hence it can be

accompanied along with other traditional treatment of OSMF. It can be drawn from the literature that successful outcome of the adjuvant therapies in management of oral sub mucous fibrosis, but there is inadequate evidence for definitive form of treatment. Therefore, appropriate studies need to be reviewed to increase understanding of adjuvant therapy for treatment of OSMF.

REFERENCES

- [1]. Pindborg JJ, Sirsat SM. Oral submucous fibrosis. *Oral Surg* 1966;22:764.
- [2]. Pindborg JJ, Chawla TN, Srivastava AN, Gupta D. Epithelial changes in oral submucous fibrosis. *Acta Odon Scandinav* 1965;23:277-86.
- [3]. Khan S, Sinha A, Kumar S, Iqbal H. Oral submucous fibrosis: Current concepts on aetiology and management—A review. *Journal of Indian Academy of Oral Medicine and Radiology*. 2018 Oct 1;30(4):407-11.
- [4]. Asha V, Baruah N. Physiotherapy in treatment of oral submucous fibrosis related restricted mouth opening. *International Healthcare Research Journal*. 2017 Nov 10;1(8):252-7.
- [5]. More CB, Das S, Patel H, Adalja C, Kamatchi V, Venkatesh R. Proposed clinical classification for oral submucous fibrosis. *Oral oncology*. 2012 Mar 1;48(3):200-2.
- [6]. Kerr AR, Warnakulasuriya S, Mighell AJ, Dietrich T, Nasser M, Rimal J, Jalil A, Bornstein MM, Nagao T, Fortune F, Hazarey VH. A systematic review of medical interventions for oral submucous fibrosis and future research opportunities. *Oral diseases*. 2011 Apr;17:42-57.
- [7]. Warnakulasuriya S, Johnson NW, Van der Waal I. Nomenclature and classification of potentially malignant disorders of the oral mucosa. *Journal of oral pathology & medicine*. 2007 Nov;36(10):575-80.
- [8]. Aziz SR. Oral submucous fibrosis: an unusual disease. *Journal of the New Jersey Dental Association*. 1997 Jan 1;68(2):17-9.
- [9]. Jp C. Oral submucous fibrosis: its pathogenesis and management. *Br Dent J*. 1986;160:429-34.
- [10]. Pindborg JJ, Mehta FS, Daftary DK. Occurrence of epithelial atypia in 51 Indian villagers with oral submucous fibrosis. *British journal of cancer*. 1970 Mar;24(2):253-7.
- [11]. Sambandan TJ. Medical Treatment Modalities of Oral Sub Mucous Fibrosis. *Natl J Integr Res Med*. 2011;3:147-51.

- [12]. Srivastava A, Agarwal R, Singh OP. Clinical evaluation of the role of tulsi and turmeric in the management of oral submucous fibrosis: A pilot, prospective observational study. *J Ayurveda Integr Med.* 2015;6(1):45–9.
- [13]. Arreola R, Quintero-Fabián S, López-Roa RI, et al. Immunomodulation and anti-inflammatory effects of garlic compounds. *J Immunol Res.* 2015;2015:401630
- [14]. Gautam, Nandita & KK, Shivalingesh & Verma, Satyaki. (2020). NON PHARMACOLOGICAL APPROACH FOR TREATMENT OF OSMF- A REVIEW. *International Journal of Ayurveda and Pharma Research.* 80-83. 10.47070/ijapr.v8i7.1498.
- [15]. Devi, Mutum & J, Manju & Rajpurohit, Rahul & Sophia, Khumukcham & Sorokhaibam, Binita. (2020). Adjuvant therapy for oral submucous fibrosis. *International Journal of Oral Health Dentistry.* 6. 78-80. 10.18231/j.ijohd.2020.018.
- [16]. Prakash P, Misra A, Surin WR, Jain M, Bhatta RS, Pal R, Raj K, Barthwal MK, Dikshit M. Anti-platelet effects of Curcuma oil in experimental models of myocardial ischemia-reperfusion and thrombosis. *Thrombosis research.* 2011 Feb 1;127(2):111-8.
- [17]. Kuttan R, Sudheeran PC, Josph CD. Turmeric and curcumin as topical agents in cancer therapy. *Tumori Journal.* 1987 Feb;73(1):29-31.
- [18]. Agarwal N, Singh D, Sinha A, Srivastava S, Prasad RK, Singh G. Evaluation of efficacy of turmeric in management of oral submucous fibrosis. *Journal of Indian Academy of Oral Medicine and Radiology.* 2014 Jul 1;26(3):260-3.
- [19]. Sharma OP. Antioxidant activity of curcumin and related compounds. *Biochemical pharmacology.* 1976 Aug 1;25(15):1811-2.
- [20]. Sudarshan R, Annigeri RG, Vijayabala GS. Aloe vera in the treatment for oral submucous fibrosis - a preliminary study. *J Oral Pathol Med.* 2012;41(10):755–61.
- [21]. Prakash P, Gupta N. Therapeutic uses of *Ocimum sanctum* linn (Tulsi) with a note on eugenol and its pharmacological actions: A short review. *Indian J Physiol Pharmacol.* 2005;49:125–31.
- [22]. Bhattacharyya P, Bishayee A. *Ocimum sanctum* Linn. (Tulsi): an ethnomedicinal plant for the prevention and treatment of cancer. *Anticancer Drugs.* 2013;24(7):659–66.
- [23]. Agarwal R, Chaturvedi TP, Chandra A, Singh OP, Srivastava A. Clinical evaluation of the role of tulsi and turmeric in the management of oral submucous fibrosis: A pilot, prospective observational study. *J Ayurveda Integr Med.* 2015;6:45–9.
- [24]. Mulk BS, Deshpande P, Velpula N, Chappidi V, Chintamaneni RL, Goyal S. Spirulina and pentoxifylline - a novel approach for treatment of oral submucous fibrosis. *J Clin Diagn Res.* 2013;7(12):3048-3050
- [25]. Shetty P, Shenai P, Chatra L, Rao P. Efficacy of spirulina as an antioxidant adjuvant to corticosteroid injection in management of oral submucous fibrosis. *Indian J Dent Res.* 2013;24(3):347
- [26]. Chole RH, Gondivkar SM, Gadbaile AR, Balsaraf S, Chaudhary S, Dhore SV, et al. Review of drug treatment of oral submucous fibrosis. *Oral Oncol.* 2012;48(5):393–8.
- [27]. Johny J, Bhagvandas SC, Mohan SP, Punathil S, Moyin S, Bhaskaran MK. Comparison of Efficacy of Lycopene and Lycopene-Hyaluronidase Combination in the Treatment of Oral Submucous Fibrosis. *J Pharm Bioallied Sci.* 2019;11(Suppl 2):S260-S264.
- [28]. Chhabra AK, Sune R, Reche A. Oral submucous fibrosis: a review of the current concepts in management. *Cureus.* 2023 Oct 18;15(10).
- [29]. Koneru A, Hunasgi S, Hallikeri K, Surekha R, Nellithady GS, Vanishree M. A systematic review of various treatment modalities for oral submucous fibrosis. *Journal of Advanced Clinical and Research Insights.* 2014 Sep 1;1(2):64-72.
- [30]. 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.