



Review Article

Adjuvant therapy for oral submucous fibrosis

Mutum Sangeeta Devi^{1,*}, Manju J², Rahul Rajpurohit³, Khumukcham Sophia⁴,
Binita Sorokhaibam⁵

¹Dept. of Oral Medicine and Radiology, Madha Dental College and Hospital, Chennai, Tamil Nadu, India

²Dept. of Oral Medicine and Radiology, Thai Moogambigai Dental College and Hospital, Chennai, Tamil Nadu, India

³Dept. of Prosthodontics, Thai Moogambigai Dental College and Hospital, Chennai, Tamil Nadu, India

⁴Dept. of Periodontology, Dental College Jawaharlal Nehru Institute of Medical Sciences, Imphal, Manipur, India

⁵Dept. of Oral Pathology, Thai Moogambigai Dental College and Hospital, Chennai, Tamil Nadu, India



ARTICLE INFO

Article history:

Received 13-04-2020

Accepted 28-04-2020

Available online 21-07-2020

Keywords:

OSMF

Adjuvant

Curcumin

Aloe vera

Tulsi

Sesame oil

Lycopene

ABSTRACT

Oral Submucous 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 chillies. 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 curcumin, tulsi, aloe vera, spirulina, sesame oil 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 noninvasive therapeutic modality.

© 2020 Published by Innovative Publication. This is an open access article under the CC BY-NC license (<https://creativecommons.org/licenses/by-nc/4.0/>)

1. Introduction

Oral submucous fibrosis (OSMF) is a chronic precancerous condition which is characterized by juxta-epithelial inflammatory reaction and leads to progressive fibrosis of the submucosal tissues of oral cavity.¹ OSMF etiopathogenesis has not been fully understood so far, but areca nut has been reported as main etiological factor. Arecoline and Tanin found in areca nut result in an increased synthesis of collagen and decreased breakdown.² Chillies, tobacco, lime, dietary deficiency, abnormal iron metabolism, collagen disorders, bacterial infection, immunological disorders, genetic susceptibility and change in salivary composition are also found as other etiological causes.

Symptoms of OSMF differ with progression of disease. Initial signs are ulcerations of the mucosa, and 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^{3,4} results in marked stiffness and difficulty to open mouth.^{5,6} 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 subepithelial fibrosis and chronic inflammation which is followed by hyalinisation and vascular loss, parakeratosis squamous hyperplasia.^{7,8}

The various treatment protocols which have been attempted to improve the signs and symptoms of OSMF include intralesional injections of corticosteroids, placental extracts and hyaluronidase alone or in combination, laser treatment, surgical, IFN- γ , peripheral vasodilators administration, minerals, sugars, lignin, immune milk, turmeric, lycopene and micronutrient supplements. Various

* Corresponding author.

E-mail address: mutumsangeeta21@gmail.com (M. S. Devi).

physiotherapeutic modalities have also shown favourable results.⁹ Natural ayurvedic treatment along with lifestyle change can help to reduce the symptoms of OSMF and thus provide relief to the patient without having to cause side effects.¹⁰ This article provides a review of various adjuvant treatment modalities of OSMF.

2. Adjuvant Therapies

2.1. Curcumin

Curcumin is a plant-isolated polyphenol (*Curcuma longa* L.(Zingiberaceae) compound found in Southern Asia.¹¹ The exact mechanism of action and determination of bioactive materials have been examined for the medicinal properties of turmeric which is curcumin source.¹² It has three properties such as lipid peroxidation inhibition, cellular proliferation screening and inhibition of collagen synthesis.¹³ Many studies show effects curcumin in increased mouth opening of patient with OSMF.¹⁴ Studies shows improvement in mouth opening and burning sensation.¹⁵ Curcumin's antioxidant activity was reported in 1975.¹⁶ It acts as an oxygen-free radical scavenger. Curcumin has a powerful inhibitory effect in human keratinocytes and fibroblasts against H₂O₂-induced damage.¹⁷

2.2. Aloe Vera

Aloe vera works as a wound-healing hormone and serols that is highly anti-inflammatory. Sudarshan et al reported improvement of burning sensation and opening of the mouth compared with antioxidant treatment.¹⁸ Aloe vera contains 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. Bradykinase 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, immunomodulatory and gastro-protective properties. Properties of aloe vera suggest the possibility of its use in the management of OSMF.¹⁹

2.3. Tulsi

Tulsi increases immunity and enhances metabolism. It is an extract which has been found inhibiting enzymes to reduce inflammation. It is also decreasing depression and exhibits antioxidant properties.^{20,21} It has antioxidant, anti-inflammatory, chemo-preventive, anticarcinogenic and immunomodulatory etc.^{10,22} According to Adit Srivastava et al., the synergistic activity of tulsi has resulted in greater effectiveness and highly effective anti-OSMF therapy. During the first month of testing, it triggered an early, prolonged and substantial decrease during burning

sensation, both clinically and statistically. Mouth opening has also changed significantly. In extreme cases, the findings were better representing its greater efficacy.²³

2.4. Sesame oil

Sesame plant (*Sesamum indicum/tila*) is Pedaliaceae family which was considered a gift of nature to mankind due to its nutritious properties and other beneficial health effects. The seeds are known as "gingelly" or "til". It is a good source of vitamin E with high concentration of polyunsaturated fatty acids and contains antioxidants namely sesamol, sesamin and sesamol which help in treatment of OSMF.²

2.5. Spirulina

It is microalgae, found in native of African and American everyday diets. It contains phenolic acid, tocopherols and beta-carotene with antioxidant properties. Spirulina has been used with positive results in treating many oral mucosal lesions.²⁴ According to Shetty P et al spirulina shows the effective result in treating OSMF patients.²⁵ Use of spirulina in the successful management of OSMF is attributed to its antioxidant, anti-inflammatory and immuno-modulating properties.²⁶ The blue green algae, spirulina is rich in carotenoids and other micronutrients possessing chemo preventive potential. It has been used to test the clinical activity in reversing the oral precancerous lesions like leukoplakia.²⁷

2.6. Lycopene

Lycopene is bright red carotene with carotenoid pigment found in fruits and vegetables including tomatoes, apricots, papaya, watermelon, carrots and other fruits of yellow colour. Through maintaining essential cellular biomolecules including lipids, lipoproteins, proteins and DNA, it helps in preventing carcinogenesis and atherogenesis. It is the most effective biological antioxidant agent which is also used in treatment of OSMF.^{28,29} Studies has reported statistically significant of lycopene supplement at a daily dose in improving patients with oral submucous fibrosis.³⁰

3. 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 used along with traditional treatment of OSMF. Even literature supports the successful outcome of the adjuvant therapies in management of oral submucous 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.

4. Financial Support and Sponsorship

Nil.

5. Conflicts of Interest

There are no conflicts of interest.

References

- Pindborg JJ, Sirsat SM. Oral submucous fibrosis. *Oral Surg Oral Med, Oral Pathol.* 1966;22(6):764.
- Tilakaratne WM, Klinikowski MF, Saku T, Peters TJ, Warnakulasuriya S. Oral submucous fibrosis: Review on aetiology and pathogenesis. *Oral Oncol.* 2006;42(6):561–8.
- More CB, Das S, Patel H, Adalja C, Kamatchi V, Venkatesh R. Proposed clinical classification for oral submucous fibrosis. *Oral Oncol.* 2012;48(3):200–2.
- Kerr AR, Warnakulasuriya S, Mighell AJ, Dietrich T, Nasser M, Rimal J. A systematic review of medical interventions for oral submucous fibrosis and future research opportunities. *Oral Diseases.* 2011;17:42–57.
- Warnakulasuriya S, Johnson NW, Waal IVD. Nomenclature and classification of potentially malignant disorders of the oral mucosa. *J Oral Pathol Med.* 2007;36(10):575–80.
- Aziz SR. Oral submucous fibrosis: an unusual disease. *J N J Dent Asso.* 1997;68:17–19.
- Canniff JP, Harvey W, Harris M. Oral submucous fibrosis: its pathogenesis and management. *Br Dent J.* 1986;160(12):429–34.
- Pindborg JJ, Mehta FS, Daftary DK. Occurrence of Epithelial Atypia in 51 Indian Villagers with Oral Submucous Fibrosis. *Br J Cancer.* 1970;24(2):253–7.
- Sambandan TJ. Medical Treatment Modalities of Oral Sub Mucous Fibrosis. *Natl J Integr Res Med.* 2011;3:147–51.
- 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.
- Sandur SK, Ichikawa H, Pandey MK, Kunnumakkara AB, Sung B, Sethi G, et al. Role of pro-oxidants and antioxidants in the anti-inflammatory and apoptotic effects of curcumin (diferuloylmethane). *Free Radic Biol Med.* 2007;43:568–80.
- Prakash P, Misra A, Surin WR, Jain M, Bhatta RS, Pal R, et al. Antiplatelet effects of Curcuma oil in experimental models of myocardial ischemia-reperfusion and thrombosis. *Thromb Res.* 2011;127(2):111–18.
- Suryanarayana P, Krishnaswamy K, Reddy GB. Effect of curcumin on galactose-induced cataractogenesis in rats. *Mol Vis.* 2003;9:223–30.
- Kuttan R, Sudheeran PC, Josph CD. Turmeric and Curcumin as Topical Agents in Cancer Therapy. *Tumori J.* 1987;73(1):29–9.
- Agarwal N. Evaluation of efficacy of turmeric in management of oral [21] submucous fibrosis. *J Indian Acad Oral Med Radiol.* 2014;26(3):260–3.
- Sharma OP. Antioxidant activity of curcumin and related compounds. *Biochem Pharmacol.* 1976;25:1811–2.
- Ruby AJ, Kuttan G, Babu KD, Rajasekharan KN, Kuttan R. Antitumour and antioxidant activity of natural curcuminoids. *Cancer Lett.* 1995;94(1):79–83.
- 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.
- Dwivedi N, Agarwal A. Aloe vera: Magic or myth. *SRM J Res Dent Sci.* 2013;4(3):119.
- 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.
- Kelm MA, Nair MG, Strasburg GM, DeWitt DL. Antioxidant and cyclooxygenase inhibitory phenolic compounds from Ocimum sanctum Linn. *Phytomed.* 2000;7(1):7–13.
- 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.
- 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.
- Miranda MS, Cintra RG, Barros SBM, Mancini-Filho J. Antioxidant activity of the microalga *Spirulina maxima*. *Braz J Med Biol Res.* 1998;31(8):1075–9.
- 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.
- Chole RH, Gondivkar SM, Gadail AR, Balsaraf S, Chaudhary S, Dhore SV, et al. Review of drug treatment of oral submucous fibrosis. *Oral Oncol.* 2012;48(5):393–8.
- Mathew B, Sankaranarayanan R, Nair PP, Varghese C, Somanathan T, Amma BP, et al. Evaluation of chemoprevention of oral cancer with spirulina fusiformis. *Nutr Cancer.* 1995;24(2):197–202.
- Lu R, Dan H, Wu R, Meng W, Liu N, X J. Lycopene: Features and potential significance in the oral cancer and precancerous lesions. *J Oral Pathol Med.* 2011;40:361–8.
- Saawarn N, Saawarn S, Chaitanya NC, Shashikanth MC, Jirge V, Pinakapani R. Lycopene in the management of oral lichen planus: A placebo-controlled study. *Indian J Dent Res.* 2011;22(5):639–43.
- Kumar A, Bagewadi A, Keluskar V, Singh M. Efficacy of lycopene in the management of oral submucous fibrosis. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod.* 2007;103(2):207–13.

Author biography

Mutum Sangeeta Devi Senior Lecturer

Manju J Senior Lecturer

Rahul Rajpurohit Senior Lecturer

Khumukcham Sophia Assistant Professor

Binita Sorokhaibam Post Graduate Trainee

Cite this article: Devi MS, Manju J, Rajpurohit R, Sophia K, Sorokhaibam B. Adjuvant therapy for oral submucous fibrosis. *Int J Oral Health Dent* 2020;6(2):78-80.