

Alternative Therapies In OSMF

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Introduction

Oral submucous fibrosis (OSMF) is a chronic, insidious oral mucosal condition that occurs predominantly among Indians and occasionally in other Asians especially Taiwanese and sporadically in Europeans. It was first described by Pindborg and Sirsat.⁸ It is considered as a potentially malignant disorder. Although the pathogenesis of the disease is thought to be multifactorial, chewing of betel quid/areca nut has been recognized as one of the most significant risk factors for OSMF.¹

Worldwide estimate of OSMF indicates that 2.5 million people are affected with most cases connected on the Indian subcontinents, especially southeast India.^{2,3}

The hallmark of the disease is submucosal fibrosis that affects the oral cavity and progressively involves the pharynx and the upper oesophagus. It is characterized by juxta-epithelial inflammatory reaction followed by a chronic change in the fibro-elasticity of the lamina propria and is associated with epithelial atrophy. This leads to burning sensation in the oral cavity, blanching, and stiffening of oral mucosa and oropharynx, resulting in restricted mouth opening which in turn causes limited food consumption, difficulty in maintaining oral health, and impairs the ability to speak.^{1,4}

OSMF is one of the most poorly understood and unsatisfactorily treated disease. All available treatments give the patient only symptomatic relief, which is short lived. This is mainly because the aetiology of the disease is not fully understood and the disease is progressive in nature. The younger the age, the more rapid is the progression of the disease, and more likely is the recurrence of symptoms.⁵ Wide range of medical and surgical attention has been attributed towards the management of OSMF. However, there is no complete remission till date. The symptomatic medical treatment is predominantly aimed at improving mouth movements and secondly improving the health of individual. Specific treatment includes administration of steroids, lycopene, surgical

excision, lasers, etc. The failure to achieve proper or specific treatment and with all the ill-effects associated with these conventional / traditional medicines, there is a need for utilization of alternative therapies as a modality/adjuvant to the traditional approaches. Alternative therapies include the use of herbs like aloe vera and curcumin, ayurvedic medicines, naturopathy including use of Spirulina are the new ray of hope in the management of OSMF.

In recent years, various studies have been done using these alternative modality as a main treatment option or as an adjuvant to other therapies, which showed improvement comparable to the conventional treatment and has appeared to be promising in management of OSMF with minimal side effects and contraindications. So, this review presents a spectrum of alternative treatment modalities for management of oral submucous fibrosis and their rationale.

Aloe Vera

The plant Aloe vera has a history dating back to biblical time. The Aloe vera plant has been known and used for centuries for its health, beauty, medicinal and skin care properties. The Aloe vera is complex. The plant contains vitamins A, C and F. Vitamin B (thiamine), niacin, vitamin B2 (riboflavin), choline and folic acid along with traces of vitamin B12. Enzymes such as acid phosphatase, alkaline phosphatase, amylase, lactic dehydrogenase and lipase. When taken orally, these biochemical catalysts, amylase and lipase aid in digestion by breaking down fats and sugars. It consists of 75 different ingredients, including vitamins, minerals, enzymes, sugars, anthraquinones or phenolic compounds, lignin, saponins, sterols, amino acids and salicylic acid. Yamaguchi et al reported the presence of aluminum, sodium, potassium, calcium, magnesium, manganese, copper, zinc, chromium and iron in the aloe plant.⁶

Aloe Vera is a mannoprotein containing many amino acids known as 'wound healing hormones'. The polysaccharides contained in the gel of the leaves, promote wound healing and have anti-inflammatory, immunomodulatory, antioxidant, and gastroprotective properties. Sterols in Aloe vera have strong ability to inhibit inflammation similar to the action of cortisone without any side effects.⁷

Sudarshar R et al evaluated the efficacy of Aloe vera to antioxidants capsules in the treatment for OSMF. Aloe vera showed a statistically significant reduction in burning sensation ($P = 0.008$), improvement in mouth opening ($P = 0.02$), and cheek flexibility ($P = 0.01$) on comparing with the antioxidant group.⁷ Anuradha A et al evaluation of efficacy of aloe vera in the treatment of OSMF as a lone

modality compared to steroid. The clinical response to aloe vera was comparable to that of intralesional injections of hydrocortisone and hyaluronidase with antioxidant supplementation. The study concluded that Aloe vera can be an alternative, safe, and effective treatment regime in the management of OSMF.⁸

Curcumin

Curcumin is a natural dye isolated from the root and stalk of turmeric, also known as: Yellowroot/Zingiberaceae lat. *Curcuma longa*/domestica, *Curcuma manga*. Curcumin has a potent anti-inflammatory activity and many clinical trials has proved it. There are two pathways of inflammation: cyclooxygenase pathway by which prostaglandins are formed from arachidonic acid and lipoxygenase pathway by which pro-inflammatory leukotrienes are formed from the same. Curcumin downregulates both the mechanisms, both at the transcriptional level as well as via post-translational enzyme inhibition. Apart from that, curcumin, a pleiotropic molecule, has the capability to interact and restrain many molecules associated with inflammation. Curcumin also inhibits inflammatory cytokines i.e. tumor necrosis factor-alpha (TNF- α), interleukin (IL) -1, -2, -6, -8, and -12, monocyte chemoattractant protein (MCP), and migration inhibitory protein etc. through various mechanisms.⁹

Curcumin is a strong antioxidant, both in vitro and in vivo. Various studies have demonstrated its effectiveness in decreasing the oxidative stress and scavenging free radicals. The presence of methylene and phenolic hydrogens and a unique conjugated structure makes it capable to perform chain breaking antioxidant actions by trapping free radicals. Apart from direct antioxidant action, curcumin also exhibits indirect antioxidant properties by potentiating the other antioxidant systems of body. Curcumin is an important anticancer agent and its anticancer potential is studied in multiple human carcinomas including melanoma, head and neck, breast, colon, pancreatic, prostate and ovarian cancers. It induces apoptosis in cancer cells. It causes suppression of certain oncogenes, inhibition of chromosomal damage, inhibition of tumor implantation, inhibition of tyrosine kinase activity and inhibition of biotransformation of carcinogenesis.⁹

OSMF is one of the most commonly encountered PMD. Due to its antioxidant, anticancerous and anti-inflammatory properties, curcumin plays a key role in the treatment of this disease. Treatment with curcumin helps in reducing the burning sensation and in improving the mouth opening in the patients with OSMF. Rai B et al conducted a study in which 25 patients with OSMF treated with curcumin

showed significant decrease in burning sensation and improvement in mouth opening.¹⁰ Vinay K conducted randomized clinical trial efficacy of curcumin to Tenovate ointment (clobetasol propionate (0.05%) in the treatment for OSMF. Curcumin group showed 5.93 (± 2.37) mm increase in mouth opening compared to 2.66 (± 1.76) mm of the control group. It is evident from the study that curcumin holds good promise in the treatment of OSMF in future.¹¹

Spirulina

Spirulina refers to the dried biomass of *Arthrospira platensis*, an oxygenic photosynthetic bacterium found worldwide in fresh and marine waters. It grows naturally in alkaline waters of lakes in warm region.^{12,13} Spirulina is rich in protein, vitamins, minerals, and carotenoids, antioxidants that can help protect cells from damage. It contains nutrients, including B complex vitamins, beta-carotene, vitamin E, manganese, zinc, copper, iron, selenium, and gamma linolenic acid (an essential fatty acid).¹⁴

The aqueous extract of spirulina was found to have a major impact on the immune system by increasing the phagocytic activity of macrophages, stimulating the NK cells. It also played a role in the activation and mobilization of T and B cells due to its stimulatory effects in the production of cytokines and antibodies. Spirulina contains several active ingredients, notably phycocyanin and β -carotene that have potent antioxidant and anti-inflammatory activities. Phycocyanin has the ability to scavenge free radicals, including alkoxyl, hydroxyl and peroxy radicals. As anti-inflammatory activities, phycocyanin inhibits pro-inflammatory cytokine formation, such as TNF α , suppresses cyclooxygenase-2 (COX-2) expression and decreases prostaglandin E(2) production. Another ingredient of Spirulina, β -carotene, has been reported to have antioxidant and anti-inflammatory activities.^{14,15}

Spirulina has been used for the treatment of several oral mucosal lesions with successful results. It has been primarily assessed in treating leukoplakia, OSMF with promising results. The antioxidant, anti-inflammatory, immunomodulatory & chemo-preventive, property of spirulina makes it as one of the new treatment modality in OSMF.^{15,16}

Bhawna SM, et al conducted a study to assess the efficacy of spirulina and Pentoxifylline. Pentoxifylline and Spirulina showed promising results in treatment of Oral sub mucous fibrosis. Spirulina was used for the first time for treatment of Oral sub mucous fibrosis (OSMF) and it proved to be superior than Pentoxifylline as no side effects were observed.¹⁷ Santosh Patil et al conducted a study to compare the efficacy of spirulina and lycopene in the management of OSMF. Clinical improvements in mouth opening was significant with lycopene whereas ulcers/erosions/vesicles significantly improved with Spirulina.¹⁸

Conclusion

A long time span has passed since the first diagnosis of OSMF and a wide range of medical

Zeba et al., Alternative Therapies In OSMF

and surgical attention has been attributed towards the management of the same. However, there is no complete remission until date. Alternative therapies including use of herbs like aloe vera, curcumin, Ayurvedic medicine and its therapies like oil pooling, physical therapies involving use of therapeutic ultrasound, microwave diathermy are the new ray of hope in the management of OSMF. Aloe vera, Curcumin and Spirulina having wide range of biological properties like antioxidant, anti-inflammatory, anti-cancer, immune-modulatory effect and various nutritional benefits appears to be an effective modality in its management. In recent years, various studies have been done using these alternative modality as a main treatment option or as an adjuvant to other therapies, which showed improvement comparable to the conventional treatment and has appeared to be promising in management of OSMF with minimal side effects and contraindications. A more extensive clinical trials involving a greater number of cases and high-quality randomized controlled trials should be initiated and clinicians should encourage the use of these alternative treatment modalities.

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