

Drug Treatment of Oral Sub Mucous Fibrosis – A Review

Revant H. Chole¹, Ranjtkumar Patil²

ABSTRACT

Oral submucous fibrosis (OSMF) is a potentially malignant disease that results in progressive juxtaepithelial fibrosis of the oral soft tissues, resulting in increasing loss of tissue mobility, marked rigidity and an eventual inability to open the mouth. The treatment of oral submucous fibrosis includes iron, multivitamins including lycopene, spirulina, pentoxifylline, local submucosal injections of steroids, hyaluronidase and chylomicrons, aqueous extract of healthy human placenta, and surgical excision of the fibrous bands.

Keywords: Oral submucous fibrosis, corticosteroids, vitamins, lycopene, spirulina.

INTRODUCTION

Oral submucous fibrosis (OSMF) is a potentially malignant disease that results in progressive juxtaepithelial fibrosis of the oral soft tissues, mainly occurring in the Indian subcontinent. It is a chronic, insidious, disabling disease involving oral mucosa, the oropharynx, and rarely, the larynx. OSMF results in an increasing loss of tissue mobility, marked rigidity and an eventual inability to open the mouth.^{1,2} The most commonly involved site is buccal mucosa, followed by palate, retromolar region, faucial pillars and pharynx.³

The etiopathogenesis of OSMF is complex and incompletely understood. The main agent involved in the pathogenesis of OSMF is areca nut. Areca nut is made up of alkaloid and flavonoid components. Four alkaloids namely arecoline, arecaidine, guvacine, and guvacoline have been identified in areca nut, of which arecoline is the most potent agent and plays a major role in the pathogenesis of OSMF by causing an abnormal increase in collagen production.

Many treatment protocols for oral sub mucous fibrosis have been proposed to alleviate the signs and symptoms of the disorder. Patient is advised to completely quit the habit of betel nut chewing. The treatment of oral submucous fibrosis includes iron, multivitamins including lycopene, pentoxifylline, local submucosal injections of steroids, hyaluronidase and chylomicrons, aqueous extract of healthy human placenta, and surgical excision of the fibrous bands.

DRUG TREATMENT

Corticosteroids

Corticosteroids are immunosuppressive agents which are believed to decrease inflammation and collagen formation, thereby reducing the symptoms and resulting in increased mouth opening. Corticosteroids such as hydrocortisone, triamcinolone, dexamethasone and betamethasone have been used in the treatment of OSMF. Steroids suppress inflammatory reactions, thereby preventing fibrosis by decreasing fibroblastic proliferation and deposition of collagen. In a study by Borle RM et al⁸ three hundred twenty-six patients with oral submucous fibrosis were divided into two groups and

treated either with conventional submucosal injections of steroids and hyaluronidase, or with topical vitamin A, steroid applications, and oral iron preparations. The results were compared. The conventional treatment with injections was found to be hazardous, whereas the conservative treatment was found to be safe. Both treatments were purely palliative. The use of processed areca nut is on the increase. In the impending danger of increased occurrence of oral submucous fibrosis and subsequent oral cancer following this habit is colossal. Another study by Ameer NT et al⁹ evaluated the effect of intralesional triamcinolone in OSMF by giving bi-weekly submucosal injections of 40 mg triamcinolone for 12 weeks and followed up for 1 year. The effect of therapy was evaluated subjectively by improvement in symptoms and objectively by increase in mouth opening.

Enzymes

Enzymes such as collagenase, hyaluronidase and chymotrypsin are being used for the treatment of OSMF. Hyaluronidase by breaking down hyaluronic acid (the ground substance in connective tissue) lowers the viscosity of intercellular cement substance. Better results are observed with respect to trismus and fibrosis. Patients receiving hyaluronidase alone showed a quicker improvement in the burning sensation and painful ulceration produced by the effects of local by-products, although combination of dexamethasone and hyaluronidase gave better long-term results than other regimens.¹⁰

In another study no statistically significant difference in sign and symptom was seen in OSMF patients between hydrocortisone acetate and hyaluronidase versus triamcinolone acetate and hyaluronidase.¹¹ Treatment regimen of group B was more convenient to the patients because less number of visits required and cheap. No side effects were seen. The authors concluded that hyaluronidase is much quicker in ameliorating painful ulceration and burning sensation than dexamethasone, but the effect is short term, although its combination with steroids gives somewhat better longer-term results.

Vitamins and minerals

Vitamins, micronutrients and minerals are effective in controlling the burning sensation and ulceration in OSMF. In one study OSMF patients received supplementation of vitamins and minerals for one to three years. Significant im-

¹PhD Scholar, ²PhD Guide. Faculty of Dental Sciences, Pacific Academy of Higher Education and Research, Udaipur, Rajasthan, India

Corresponding author: Revant Chole, A/5-203, Ruchi Lifescapes, Jatkhedhi, Hoshangabad road, Bhopal. (M.P.), India

How to cite this article: Revant H. Chole, Ranjtkumar Patil. Drug treatment of oral sub mucous fibrosis – a review. International Journal of Contemporary Medical Research 2016;3(4):996-998.

provement in symptoms, like intolerance to spicy food, burning sensation, and mouth opening, was observed at exit.¹² Vitamins A, B, C, D, E and minerals like copper, iron and magnesium stabilize and deactivate the free radicals before they attack cells. In a study by Kumar A et al¹³ oral lycopene therapy showed improvement in the signs and symptoms of OSMF. In a study by Shetty P et al¹⁴ the efficacy of spirulina as an antioxidant adjuvant to corticosteroid injections in the management of 40 OSMF subjects of south Karnataka and north Kerala was evaluated. Clinical improvements in mouth opening was significant in the posttreatment period in both Spirulina and placebo groups. Both the groups showed statistically significant reduction in burning sensation. However, when both groups were compared, mouth opening and burning sensation was found to be statistically very highly significant in favor of the spirulina group. Spirulina can bring about clinical improvements in OSMF patients and can be used as an adjuvant therapy in the initial management of OSMF patients.

Peripheral vasodilators

Vasodilators like pentoxifylline have vasodilating properties and hampered mucosal vascularity in OSMF could be increased by the use of pentoxifylline. Pentoxifylline suppresses leucocyte function and alters fibroblast physiology and stimulates fibrinolysis. In one study the effect of pentoxifylline was studied on the clinical and pathologic course of OSMF. This investigation was conducted as a randomized clinical trial incorporating a control group (Standard drug group SDG, multivitamin, and local heat therapy) in comparison to pentoxifylline test cases (Experimental drug group EDG, 400mg 3 times daily, as coated, sustained release tablets). The authors concluded that pentoxifylline can be used as an adjunct therapy in the management of oral submucous fibrosis.¹⁵ In another study Pentoxifylline 400mg for a period of 7 months, showed an improvement in total signs and symptoms of OSMF. No significant side effects were observed.¹⁶ Oral isoxsuprine as well as dexamethasone with hyaluronidase injections combined to physiotherapy showed improvement in oral submucous fibrosis. Oral isoxsuprine can be more effectively used in the treatment of OSMF.¹⁷

Other drugs

Drugs like interferon gamma (IFN-gamma) is a known anti-fibrotic cytokine. In a study by Haque MF et al¹⁸ intra-lesional IFN-gamma treatment showed improvement in the patients mouth opening from an inter-incisal distance before treatment of 21 +/- 7 mm, to 30 +/- 7 mm immediately after treatment and 30 +/- 8 mm 6-months later, giving a net gain of 8 +/- 4 mm (42%) (range 4-15 mm). In this study patients also reported reduced burning dysaesthesia and increased suppleness of the buccal mucosa.

Apart from the above therapies, immunized cow's milk has shown promising results in OSMF.¹⁹ The milk from cows immunized with human intestinal bacteria contains an anti-inflammatory component which suppresses the inflammatory reaction and modulate cytokine production in OSMF.

Ayurvedic therapy

Turmeric as a spice and household remedy has been known to be safe for centuries. turmeric oil is proved to be effective

in OSMF.²⁰ The anti-inflammatory, antioxidant and antifibrotic properties of curcumin interfere with the progression of OSMF at multiple stages in the pathogenesis of this complex disease. The antioxidative and scavenger properties of curcumin, make it a very effective chemopreventive agent in the prevention of cancer. Tea when used in combination with vitamins, with its antioxidant property can bring improvement in mouth opening in OSMF.

CONCLUSION

Management of OSMF should include counseling of patient along with lycopene/spirulina/multivitamin/minerals in the initial stages. Moderate stages of OSMF should be treated with intralesional steroids or pentoxifylline, where as advanced stages should be treated surgically.

REFERENCES

1. Warnakulasuriya S, Johnson NW, Waal I. Nomenclature and classification of potentially malignant disorders of the oral mucosa. *J Oral Pathol Med* 2007;36:575-80.
2. Aziz SR. Oral submucous fibrosis: an unusual disease. *J N J Dent Assoc* 1997;68:17-9.
3. Paissat DK. Oral submucous fibrosis. *Int J Oral Surg* 1981;10:307-12.
4. Pindborg JJ. Oral submucous fibrosis: a review. *Ann Acad Med Singapore* 1989;18:603-7.
5. Canniff JP, Harvey W, Harris M. Oral submucous fibrosis: its pathogenesis and management. *Br Dent J* 1986;160:429-34.
6. Chang YC, Hu CC, Tseng TH, Tai KW, Lii CK, Chou MY. Synergetic effects of nicotine on arecoline-induced cytotoxicity in human buccal mucosal fibroblasts. *J Oral Pathol Med* 2001;30:458-64.
7. Manoharan S, Kolanjiappan K, Suresh K, Panjamurthy K. Lipid peroxidation and antioxidants status in patients with oral squamous cell carcinoma. *Indian J Med Res* 2005;122:529-34.
8. Borle RM, Borle SR. Management of oral submucous fibrosis: a conservative approach. *J Oral Maxillofac Surg.* 1991;49:788-91.
9. Ameer NT, Shukla RK. A cross sectional study of oral submucous fibrosis in central India and the effect of local triamcinolone therapy. *Indian J Otolaryngol Head Neck Surg.* 2012;64:240-3.
10. Kakar PK, Puri RK, Venkatachalam VP. Oral submucous fibrosis--treatment with hyalase. *J Laryngol Otol.* 1985;99:57-9.
11. Singh M, Niranjana HS, Mehrotra R, Sharma D, Gupta SC. Efficacy of hydrocortisone acetate/hyaluronidase vs triamcinolone acetonide/hyaluronidase in the treatment of oral submucous fibrosis. *Indian J Med Res.* 2010;131:665-9.
12. Maher R, Aga P, Johnson NW, Sankaranarayanan R, Warnakulasuriya S. Evaluation of multiple micronutrient supplementation in the management of oral submucous fibrosis in Karachi, Pakistan. *Nutr Cancer.* 1997;27:41-7.
13. 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;103:207-13.
14. Shetty P, Shenai P, Chatra L, Rao PK. Efficacy of spirulina as an antioxidant adjuvant to corticosteroid injection

- tion in management of oral submucous fibrosis. *Indian J Dent Res.* 2013;24:347-50.
15. Rajendran R, Rani V, Shaikh S. Pentoxifylline therapy: a new adjunct in the treatment of oral submucous fibrosis. *Indian J Dent Res.* 2006;17:190-8.
 16. Mehrotra R, Singh HP, Gupta SC, Singh M, Jain S. Pentoxifylline therapy in the management of oral submucous fibrosis. *Asian Pac J Cancer Prev.* 2011;12:971-4.
 17. Bhadage CJ, Umarji HR, Shah K, Välimaa H. Vasodilator isoxsuprine alleviates symptoms of oral submucous fibrosis. *Clin Oral Investig.* 2013;17:1375-82.
 18. Haque MF, Meghji S, Nazir R, Harris M. Interferon gamma (IFN-gamma) may reverse oral submucous fibrosis. *J Oral Pathol Med.* 2001;30:12-21.
 19. Tai YS, Liu BY, Wang JT, Sun A, Kwan HW, Chiang CP. Oral administration of milk from cows immunized with human intestinal bacteria leads to significant improvements of symptoms and signs in patients with oral submucous fibrosis. *J Oral Pathol Med.* 2001;30:618-25.
 20. Joshi J, Ghaisas S, Vaidya A, Vaidya R, Kamat DV, Bhagwat AN, Bhide S. Early human safety study of turmeric oil (*Curcuma longa* oil) administered orally in healthy volunteers. *J Assoc Physicians India.* 2003;51:1055-60

Source of Support: Nil; **Conflict of Interest:** None

Submitted: 14-02-2016; **Published online:** 10-03-2016