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Oral Sub Mucous Fibrosis Current Diagnostic and Treatment Protocol

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Abstract

Oral Sub Mucous 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 sub mucous fibrosis includes iron, multivitamins including lycopene, spirulina, pentoxifylline, local sub mucosal injections of steroids, hyaluronidase and chylomicrons, aqueous extract of healthy human placenta, and surgical excision of the fibrous bands.

Keywords: Oral sub mucous fibrosis; Corticosteroids; Vitamins; Lycopene; Spirulina

Introduction

Oral sub mucous 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, retro molar 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 sub mucous fibrosis includes iron, multivitamins including lycopene, pentoxifylline, local sub mucosal 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 al. [4] three hundred twenty-six patients with oral sub mucous fibrosis were divided into two groups and treated either with conventional sub mucosal 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 sub mucous fibrosis and subsequent oral cancer following this habit is colossal.

Another study by Ameer NT et al. [5] evaluated the effect of intralesional triamcinolone in OSMF by giving biweekly sub mucosal 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 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

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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 [6].

In another study no statistically significant difference in sign and symptom was seen in OSMF patients between hydrocortisone acetate and hyaluronidase versus triamcinolone acetonide and hyaluronidase 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 [7].

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 year improvement in symptoms, like intolerance to spicy food, burning sensation, and mouth opening, was observed at exit [8].

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 al. [9] oral lycopene therapy showed improvement in the signs and symptoms of OSMF.

In a study by Shetty P et al. [10] 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 post treatment 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 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, 400 mg 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 sub mucous fibrosis [11].

In another study Pentoxifylline 400 mg for a period of 7 months, showed an improvement in total signs and symptoms of OSMF [12].

No significant side effects were observed. Oral isoxsuprine as well as dexamethasone with hyaluronidase injections combined to physiotherapy showed improvement in oral sub mucous fibrosis. Oral isoxsuprine can be more effectively used in the treatment of OSMF [13].

Other drugs like Interferon gamma (IFN-gamma) is a known anti-fibrotic cytokine. In a study by Haque MF et al intra-lesional IFN-gamma treatment showed improvement in the patients mouth opening from an inter-incisal distance before treatment of 21 mm +/- 7 mm, to 30 mm +/- 7 mm immediately after treatment and 30 mm +/- 8 mm 6-months later, giving a net gain of 8 mm +/- 4 mm (42%) (range 4 mm to 15 mm) [14].

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. 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 [15].

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 [16].

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 chemo preventive 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. Curcuma longa Linn. is commonly known as Haldi, Turmeric or Indian saffron belongs to family Zingiberaceae. Mishra et al reported that the volatile oil of Curcuma longa has effective anti-inflammatory and anti-hyaluronidase action. They suggested the antioxidative effect as evidenced by inhibition of diffusion capability of the hyaluronidase enzyme by the oil [17].

Ramsewk et al described in their study the cytotoxic, anti-inflammatory and antioxidant activity of curcumin I, II and III from Curcuma longa.

Das DA et al inferred from their study that curcumin and turmeric oil is beneficial, affordable, non invasive herbal therapy for OSMF [18].

In one clinical trial alcoholic extracts of turmeric 3 g, turmeric oil 600 mg and turmeric oleoresin 600 mg, when consumed orally, decreased the number of micro nucleated cells both in exfoliated oral mucosal cells and in circulating lymphocytes in OSMF [19].

Sudarshan R et al. [20] reported that aloe vera reduces burning sensation and improves mouth opening when applied topically in mild stage clinically and early stage histopathologically of OSMF in comparison to antioxidants from their study. It is safe, non invasive, economical, easily available and efficient in the treatment of OSMF.

Alam S et al. [21] reported that aloe vera gel was effective as an adjuvant therapy in treatment of OSMF.

Spirulina is a microalgae which contains phenolic acid, tocopherols, beta carotene and have potent antioxidant properties. Shetty P et al. [22] suggested that 500 mg spirulina twice daily can be used as an adjuvant therapy in the initial management of OSMF.

Oral mucoadhesive drug delivery is very efficient therapeutic targeted drug approach than systemic delivery, as smaller amounts of

drug can be easily dispersed at the site of the disease, thereby reducing its side effects. Mucoadhesive systems for oral local drug delivery include adhesive tablets, adhesive patches, adhesive films or pellicles, adhesive semisolid systems (gels, ointments), and adhesive liquid systems (sprays, mouthwashes).

Kumar NS et al. [23] reported semisolid mucoadhesive curcumin gel having anti turmeric and anti mutagenic property can be used for the treatment of oral sub mucous fibrosis which provides effect for extended periods of time.

Averineni RK et al. [24] conducted a preliminary study to develop mucoadhesive buccal films of valdecoxib a novel COX-2 inhibitor for the treatment of oral sub-mucous fibrosis.

The various surgical modalities chosen according to the stage of clinical progression to gain maximal Interincisal Distance (ID) includes the excision of fibrotic tissues and covering the defect with split-thickness skin, fresh human amnion, or buccal fat pad (BFP) grafts [25].

J. N. Khanna, N. N. Andrade treated advanced cases by a new surgical technique of a palatal island flap based on the greater palatine artery in combination with temporal is myotomy and bilateral coronoidectomy [26].

Bande CR et al. [27] have done the comparative study of extended nasolabial flap with the platysma myocutaneous muscle flap for reconstruction of intraoral defects after release of oral sub mucous fibrosis and revealed that both procedures are equally effective in management, but extra oral scar was not aesthetically acceptable in the nasolabial group.

Le PV et al. [28] suggested that oral stent can be used as an adjunct to prevent surgical replace. Early and postoperative rehabilitation is the most important factor in maintaining the intraoperative interincisal distance therefore psycho logic preparation of the patient before surgery plays a significant role in the success of surgery.

Huang IY et al. [29] highlighted that patient compliance is very essential to prevent the post operative surgical complications which includes patient motivation, the nature and chronicity of the disease, treatment variables, and the quality of the patient- doctor relationship.

With the advancements in medical and dental treatment protocol, the stem cell intralesional injections therapy which improves the blood circulation.

Sankaranarayanan S et al. [30] injected autologous bone marrow stem cells in 38 year old male patient with oral sub mucous fibrosis which showed significant improvement in blanching, fibrous bands and mouth opening, 4 weeks after injection.

Stephen Cox & Hans Zoellner conducted a clinical trial of physiotherapeutic treatment to improve oral opening in oral sub mucous fibrosis in the Nepali population and suggested that physiotherapy is effective for increasing the oral opening and can be readily used to improve OSF in communities with otherwise limited health resources [31].

Talsania JR evaluated the efficacy of Laser with follow-up physiotherapy to reduce trismus in OSMF and concluded that Diode laser is a less expensive and an alternative method in Asian population as it requires less hospital stay.

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.

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