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Management Strategies for Oral Submucous Fibrosis- An Update

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Author's contribution

The sole author designed, analysed, interpreted and prepared the manuscript.

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Review Article

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ABSTRACT

There are plentiful management trials in Oral Submucous Fibrosis (OSMF), such as drugs, herbs, and Chinese medicines, but none proved to be entirely successful. So in this review, there are different management strategies tried in the management of OSMF, mechanism of action, and the dosage regimen.

Keywords: Oral submucous fibrosis (OSMF); potentially malignant disorder; management.

1. INTRODUCTION

Oral submucous fibrosis (OSMF) is a chronic disease associated with significant functional morbidity and an increased risk for malignancy. OSMF predominantly affects the Asian population and Asian migrants living in other parts of the World [1].

But in most of the research the management of OSMF was based on Clinical, Histopathological and fuctional staging proposed by several authors [2].

The management of OSMF has been discussed previously by several authors [3,4,1]. This Review updates the different management protocols available and tried for OSMF.

2. VARIOUS MANAGEMENT OF OSMF IS CATEGORIZED AS FOLLOWS

1. Habit counseling
2. Basic regimen
3. Medical management
4. Physiotherapy

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Table 1. Different drugs tried as management protocols are discussed in the table

Sl no	Drugs	Mechanism of action	Duration	Dosage	Route of administration
		STEROIDS			
1.	Hydrocortisone [8]	Anti-inflammatory action by inhibiting the generation of inflammatory factors and increasing the apoptosis of inflammatory cells.[2]	once a week for 12 weeks	1.25 cc of injection hydrocortisone on each side	Intralesional
2.	Dexamethasone [9]		10 weeks	4 mg	Intralesional
3.	Triamcinolone acetonide [10]		Divided doses at 10 day intervals for a period of 2 -3months	150-200 mg	Intralesional
4.	Triamcinolone diacetate [11]		4 weeks	10 mg/ml	Intralesional
5.	Betamethasone [11]		6 hours for 3 weeks	0.5 mg/ml	Topical
6.	Prednisolone [12]		2-4 weeks	20-30 mg	Systemic
7.	Steroids and Physiotherapy [8].	Microwave diathermy at 2450 MC/s and injection of hydrocortisone, vitamin A and B complex.	20 minutes with 15 sittings	20-25 Watts	Selective heating of Juxtaepithelial connective tissue Madalli V et al.,2014)
		NUTRITIONAL SUPPLEMENTS			
8.	Vitamins and minerals [13]	The main action is eliminating the deficiency status and normalizing the cellular activity to prevent pathological mechanisms like carcinogenesis. *The hypothesis of vitamin E mechanism* 1. Preventing the formation of oxidation products. 2. Free radical scavenger Prevent nerve-related pathologies 3. Increase the life span of erythrocytes	6 weeks	Beta Carotene 50mg, vitamin A palmitate 2500 IU, vitamin E acetate, 10 IU with vitamin C, zinc, copper and manganese	oral
9	Thioctic acid [14].	Antioxidant	30 min before or 2 hours after food	600-1800 mg daily. Iv Dose 300-600 mg	
		BIOGENIC STIMULATORS			
10	Placental extracts[9]	It is an aqueous extract of the human placenta that contains nucleotides, enzymes, vitamins, amino acids, and steroids. The mechanism through **"**biogenic stimulation, and by increasing the recovery [15].	10 weeks	2 cc	Intralesional

Sl no	Drugs	Mechanism of action	Duration	Dosage	Route of administration
11.	Papain and urea [16]	Proteolytic enzymes breakdown the inappropriate connective tissue fibrosis [1].	2 to 3 times daily for 15 days	100 gms urea and 100 gms papain	Intraoral
		ENZYMES			
12.	Chymotrypsin [9]	Proteolytic enzymes breakdown the inappropriate fibrosis [1].	Biweekly	5000 IU	Intralesional
13.	Hyaluronidase [9]		Biweekly for 10 weeks	1500 IU	Intralesional
14.	Collagenase [17]		once a week for 6 weeks	1 ml of collagenase (1% solution) mixed with 1 ml of xylocaine	Intralesional
		PENETRATION ENHANCERS			
15.	Borneol [18]	Anti-fibrosis activity inhibits fibroblasts mitosis, collagen, and TIMP-1 production and can be used as a penetration enhancer [18].	Incubation period of 24,48 and 72 hours.	serial dilution of borneol (18.75, 37.5, 75, 150–300 lg／ml)	Penetration enhancing effects tried in mice fibroblast Invitro study
		VASODILATORS			
16.	Nylidrin hydrochloride [19]	Nylidrin relaxes and dilates the blood vessel ensures more excellent blood supply to ischemic tissues with little or no change in the blood pressure and heart rate [19].	3-8 weeks	6 mg	Oral
17.	Pentoxifylline [20]	It is a methylxanthine derivative with vasodilating properties and was envisaged to increase mucosal vascularity Rajendran et al., [20].	3 times daily for 7 months	400mg	Oral
18.	Buflomedial hydrochloride [21]	The mechanism is through vasodilation, mild anticoagulant properties, immune modulation, and antioxidant properties have been reported [1].	4 weeks	450 mg TID	Oral
19.	xantinol nicotinate [22]	Peripheral vasodialator	4 months	Biweekly	Intralesional
		IMMUNOMODULATORS			
20.	Levamisole and vitamin A [23]	Immune modulation diminishes pro-fibrotic inflammation and enhances pro-fibrinolytic immune-mediated pathways [1].	4 days OD for one week followed by biweekly for one month	150 mg of levamisole along with aqua sol caps 50000 iµ	Oral
21.	Interferon gamma [24]	*IFN γ* is an antifibrotic cytokine.	Twice a week for 8 weeks(15 intralesional injections)	Eutectic Mixture of Local Anesthetics cream for 15 minutes then followed by IFN-	Intralesional

Sl no	Drugs	Mechanism of action	Duration	Dosage	Route of administration
				application of 0.25 ml (50 mg) of	
		ALTERNATIVE MEDICINE			
22.	Immune milk [25]	It contains a highly active anti-inflammatory compound that suppressed the experimentally induced inflammation in animal models.	Twice a day for 3 months	45 gm	Oral
23.	Turmeric [26]	Anti-inflammatory, antioxidant, anti-cancer properties.	3 months	Turmeric Oil (600 mg TO mixed with 3 g Extracts of Turmeric/day)	Oral
24.	Lycopene [27]	Anticarcinogenic, antioxidant, highest physical quenching	2 months	16 mg	Oral
25.	Tea pigments and vitamins [28]	The main action is by eliminating the deficiency status and normalizes the cellular activity to prevent pathological mechanisms like carcinogenesis [1].	????	?????	????
26.	Mangifera indica, Withania somnifera, Daucus carota, Glycyrrhiza glabra, Vitis vinifera, Emblica officinalis, Yashada bhasma, oils of Triticum sativum [22]	Herbal antioxidant formulation.	3 months	2 capsules Mangifera indica-94 mg, Withania somnifera-71 mg, Daucus carota-47 mg, Glycyrrhiza glabra-29 mg, Vitis vinifera-12 mg, Emblica officinalis-141 mg, Yashada bhasma-2.5 mg, oils of Triticum sativum 6.5 mg [29]	Oral
27.	Aloe vera [30]	Antioxidant, anti-inflammatory, and immunomodulation	3 times daily for 3 months	5 mg gel	Topical
		OTHERS			
28.	Gold, Iodine and Arsenotyphoid [31]	With the surgical cutting of bands, Large Internal doses and Injection respectively			
29.	Glucosidorum tripterygii totorum, vitamin A and E, nicotinic acid [32]	The main action is by eliminating the deficiency status and normalizes the cellular activity to prevent pathological mechanisms like carcinogenesis [1].			
30.	Danxuan koukang, salvia miltiorrhiza [33]	The mechanism is through vasodilation, mild anticoagulant properties, immune modulation, and antioxidant properties have been reported [1].			

Sl no	Drugs	Mechanism of action	Duration	Dosage	Route of administration
31.	Turmeric and black pepper [34]	Anti-inflammatory, antioxidant, anticarcinogenic, antifibrotic, immunomodulatory	3 months	Turmeric 400 mg Black pepper 100 mg 2 capsules TID	Oral
32.	Nigella sativa [34]	Anti-inflammatory, antioxidant, anticarcinogenic, antifibrotic, immunomodulatory	3 months	500 mg 2 capsules TID	Oral
33.	Spirulina in combination with isometric exercises/threaded tapered screw/mouth stretching device [35]	antioxidant, anti- inflammatory and immuno-modulation	3 months	BID	Oral
34.	Pentoxifylline and garlic pearls [36]	Garlic has immunomodulation, vasodilator, antioxidant, anti-inflammatory, and chemopreventive Pentoxifylline has antifibrinolytic, immunomodulation, anti-TNF effect, and hemorheological properties.	3 months	Pentoxifylline 400 mg and garlic pearls 0.25% BID	Oral

4. Surgical management
5. Laser Management

2.1 Habit Counseling

The first and foremost treatment plan in OSMF is strict discontinuance of habit with motivation and intense councelling session for educating and creating awareness about the disease and its malignant potential [5].

2.2 Basic Regimen

The second line of approach for the management of OSMF is the nutritional supplementation like Vitamins and Iron. It has been observed in a study that majority of the OSMF patients has Vitamin B12 and Iron deficiency due to inability to eat [6].

2.3 Medical Management

The management of OSMF has significant challenges for treatment options. Even Though several options are available still an established treatment regimen is lacking. So such treatment options available are discussed in Table 1. The medical management strategies are categorized with following heading as steroids, nutritional supplements, biogenic stimulators, enzymes, penetration enhancers, vasodilators, immunomodulators, alternative medicine and others. Future therapies suggested are molecular targeted therapies, Imatinib, Pirfenidone, nintedanib, Clostridium histolyticum collagenases, Simtuzumab, Hyperbaric Oxygen therapy, and personalized Medicine [7].

2.4 Physiotherapy

Physiotherapy over the affected area to generate heat and mouth opening has been tried. A study in 2009 conducted on Fifty-four Nepali OSMF patients was managed for four months by randomly assigning them to 3 groups. The first group of patients in the physiotherapy group were asked to do jaw exercises five times a day in which tongue spatulas were placed passively between anterior teeth, spatula number determined by comfortable mouth opening. An extra spatula was added every fifth day, but the spatula was tried on the tenth day in case of pain. The patient was subjected to analgesics 30 minutes before exercise to reduce the pain. The second group was treated with local injection of steroids, and the third group received no active treatment. The patients subjected to physiotherapy improved mouth opening compared to the other two groups [37].

2.5 Surgical Treatment

This form of modality is usually suggested during the severe form of OSMF and when the other forms of modality are unsuccessful. The common method of excision is scalpel which is considered to be the preparatory step for surgical treatment. Different surgical procedures tried are intraoral (tongue, palate, buccal fat pad), extraoral (temporal fascia, nasolabial), distant flaps, grafts, muscle myotomies and oral stents etc. Further a systematic review stated that the choice of procedure depends on the operator. [38].

2.6 Laser

A systematic review by Gondivkar SM et al. from various databases found that studies with Laser were used for stage II and III OSMF patients. Even though different Laser types and parameters were considered, all studies showed improvement in mouth opening ranging between 6.84mm to 23.7mm. Further two studies showed improvement in tongue protrusion, check flexibility, and reduction in burning sensation [39].

3. CONCLUSION

The treatment of OSMF is still not satisfactory. Therefore, further clinical trials with newer modalities and combinations are required to manage this potentially malignant disorder and to prevent its malignant transformation.

CONSENT

It is not applicable.

ETHICAL APPROVAL

As per international standard or university standard ethical approval has been collected and preserved by the authors.

COMPETING INTERESTS

Author has declared that no competing interests exist.

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