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A SYMBIOSIS OF PHOTOCEUTICLE AND PHARMACEUTICAL THERAPY IN THE MANAGEMENT OF ORAL SUBMUCOUS FIBROSIS: A CASE REPORT

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ABSTRACT

One of the most common potentially premalignant condition in India is Oral submucous fibrosis (OSMF) with 3-6% of malignant transformation. Habits of betel nut, tobacco, smoking, and pan masala have shown a close association with the occurrence of OSMF. The characteristic feature of OSMF is the progressive hyalinization of the submucosa leading to reduced mouth opening. Various treatment modalities including drug therapy, surgical therapy, and physiotherapy have been proposed till date for the management of OSMF although optimal doses of local injection with corticosteroids, hyaluronidase, and local anesthesia had shown significant reduction in the clinical symptoms. As photobiomodulation is an emerging minimally invasive therapy which can utilized for the treatment of OSMF thorough its anti- inflammatory and analgesic effect. This article is to report a case of OSMF, which was treated with a combination therapy of photobiomodulation and intralesional injection of triamcianalone acetonide and hyaluronidase and gave better results in terms of improved mouth opening and reduction in burning sensation.

INTRODUCTION

The evolution of oral submucous fibrosis (OSMF) is well documented since Sushruta, one of India's greatest physicians and named it "Vidari."[1] The Indian subcontinent is where this disorder is most common. The first person to describe OSMF in India was Joshi in 1953.[2] With a 3–6% incidence of malignant transformation in advanced OSMF cases, oral submucous fibrosis is one of the most poorly understood and inadequately treated condition.[3]

JJ Pindborg defined OSMF as "an insidious chronic disease affecting any part of the oral cavity and sometimes the pharynx. Although occasionally preceded by and /or associated with vesicle formation, it is always associated with juxta epithelial inflammatory reaction followed by a fibro elastic change of lamina propria, with epithelial atrophy leading to stiffness of oral mucosa and causing trismus and inability to eat."[4]

Current epidemiological studies and evidence indicate that betel nut chewing is one of the most significant risk factors for OSMF. The most commonly encountered is areca nut alkaloid has been shown to activate buccal mucosa fibroblasts. Additionally, it can raise the levels of MMP-1 tissue inhibitors, which slows down the breakdown of collagen and promotes the formation of extracellular matrix. The buccal mucosa, the pillars of the fauces, and the entire lip circle develop thick, inelastic rope-like fibrous bands that can make it difficult to open the mouth and cause the rima oris to narrow down.[5]

Both the site and the degree of OSMF's clinical presentation vary. The severity of the illness is closely correlated with the involvement of many oral locations. The proposed new classification system by Chandiramani et al is as under.[6]

I. Clinical staging

Staging		Description
Stage 1. (S1)		Stomatitis and/or blanching of oral mucosa.
Stage 2. (S2)		Presence of palpable fibrous bands in buccal mucosa and/or oropharynx, with/without stomatitis.
Stage 3. (S3)		Presence of palpable fibrous bands in buccal mucosa and/or oropharynx, and in any other parts of oral cavity, with/without stomatitis.
Stage 4. (S4)	A.	Any one of the above stages along with other potentially malignant disorders e.g., oral leukoplakia, oral erythroplakia, etc.
	B.	Any one of the above stages along with oral carcinoma.

II. Functional staging

Staging	Description
M1.	Inter-incisal mouth opening up to or >35 mm.
M2.	Inter-incisal mouth opening between 25 mm and 35 mm.
M3.	Inter-incisal mouth opening between 15 mm and 25 mm.
M4.	Inter-incisal mouth opening >15mm.

Example – S1M1, S2M3, S2M4, S3M4, S4AM2, S4BM3

Various treatment modalities including drug therapy, surgical therapy, and physiotherapy have been proposed till date for the management of OSMF. Medical interventions include dietary supplementation with vitamins, antioxidants, corticosteroid therapy, proteolytic agents such as hyaluronidase and placental extracts and anticytokines.[7] The main goal of the treatment of OSMF is to reduce trismus and burning sensation. One of the important therapeutic modalities is intralesional injection therapy. The most commonly used intralesional agents are placental extract, corticosteroids and hyaluronidase.[8]

Colchicine is an alkaloid chemically known as colchicinum-N-acetamide. Various studies have established the role of colchicine as an antifibrotic agent by inhibiting collagen synthesis and increasing collagenolytic activity. Besides, it also has some anti-inflammatory properties. This anti-inflammatory property is related to drug's effect on polymorphonuclear leukocytes and monocyte chemotaxis, leukocyte adhesiveness, and its effect on prostaglandin E, which suppresses the leukocyte function.[9]

Photobiomodulation, previously referred to as Low-Level Laser Therapy (LLLT), biostimulation, or cold laser therapy, is frequently used in the treatment of oral disorders, such as OSMF. It speeds up the healing process, boosts immunity, repairs bones and neural tissue, and reduces pain. There have been positive outcomes from implementing PBM in dental practices to treat conditions like TMJ discomfort, trigeminal neuralgia, and muscle pain.[10]

This case report describes the OSMF patient achieved curative effects with combined treatment of Oral colchicine tablets, Intralesional injections of Triamicialone acetamide and Hyaluronidase along with the photobiomodulation.

CASE REPORT

A 27-year-old man presented to the department of periodontics with progressively limited mouth opening, dry mouth and burning sensation. The limitation of mouth opening made it difficult for his daily routine oral cleaning, speaking, and mastication. The patient had about 3 year's history of areca nut chewing, 5-6 times per day. The patient denied history of diabetes, hypertension, drug allergy history and family cancer. Oral examination showed the whitening and stiffened oral mucosa with the appearance of fibrous bands (Fig 2 and 3). The mucosa becomes markedly tough on palpation, inelastic and opaque, especially at the sites of molar region, buccal mucosa and soft palate. Marble stone appearance of palate (Fig 4) was also observed with reduced inter-incisor distance (IID) of 20 mm (Fig 5) and generalized tobacco stains on teeth. Vertical bands were palpable in both right and left buccal mucosa. Circular bands were palpable with respect to the maxillary and mandibular labial mucosa. Based on the clinical findings a diagnosis of Stage 2 M3 (S2M3) oral submucous fibrosis was made according to classification system by Chandiramani et al.[6]

TREATMENT:

The patient was educated and motivated for the cessation of the habit and informed about the treatment plan. The rest of the treatment was initiated after a complete oral prophylaxis.

Treatment protocol:

Patient was recalled for the therapy twice a week for 6 weeks which was done by the following protocol.

In the first part of the week, Photobiomodulation procedure was carried out using diode laser (Novolase Gold) 810nm, 100mW for 60 seconds delivering 6J/cm^2 in a scanning motion through a continuous mode covering the entire mucosa and palate.

In the second part of the week, hyaluronidase 1500 IU and 0.1% triamcinolone acetonide 10 mg/ml was mixed in 2 ml of lignocaine hydrochloride and was injected intralesionally (Fig 6) followed by photobiomodulation delivering 6J/cm^2 of energy (100mW for 60 seconds) (Fig 7). Patient was advised with basic physiotherapy regimen consisting of mouth exercises throughout the treatment as given by Asha et al[11](fig.1)

The whole procedure was repeated for every week till the end of the 6-week treatment regime.

Colchicine tab 0.5mg b.i.d was prescribed for 2 months.

RESULT:

At the end of 6 weeks treatment, signs of normal mucosa were evident from the earlier stiff and fibrous band of mucosa. (Fig 11 and 12) There was a gradual improvement in mouth opening with a maximum increase of about 10 mm. (First week – 22mm, second week – 23mm, third week - 25mm, fourth week - 27mm, Fifth week - 28mm and sixth week - 30mm) Fig 8-fig13. Burning sensation in the oral cavity was reduced and patient was able to eat moderately spicy food. Noticeable changes were seen in buccal mucosa as there were hardly any fibrous bands on palpation after completion of the treatment. Patient gave positive feedback regarding ability to open the mouth, improvement in speech and decreased burning sensation.

DISCUSSION

The maximum average mouth opening of 18–30 years is 56.60 mm for men and 51.04 mm for women in healthy individuals.[5] Oral mucosal patches or blanching is an important clinical feature in the early stage of OSMF. In the later stage, mouth opening limitation is caused by fibrosis of oral mucosal area.

Multiple treatment approaches for OSMF including both medical and surgical interventions have been tried. Since chewing of areca nut have been considered as one of the significant aetiologies in the pathogenesis of OSMF, the primary therapy should be cessation of habit. Hence, patients should be counselled to quit the habit. The patient here was educated about consuming tobacco and its ill effects which motivated the patient to not indulge in the habit again.

Researches using different physiotherapeutic modalities have shown to improve restricted mouth opening in OSMF patients. Physiotherapy has been used in the form of forceful mouth opening to jaw opening devices[12]

Asha et al (2017)[11] compared the efficacy of physiotherapy and intralesional injection of hyaluronidase with corticosteroid and physiotherapy alone. Physiotherapy used alone was shown to improve the mean mouth opening, tongue protrusion and cheek flexibility but was not statistically significant. But the simultaneous use of physiotherapy and intralesional injections was found to improve these parameters better than physiotherapy alone.

Colchicine has been shown to inhibit collagen synthesis. It has been reported that colchicine inhibited procollagen secretion and its conversion to collagen and thus specifically

inhibited collagen synthesis. It disrupts the microtubule formation and inhibits microtubule polymerization by binding to tubulin.[13]

Triamcinolone acetonide suppresses immune system by reducing activity and volume of lymphatic system. It heals inflammatory mucosal lesions that are responsive to steroids. It decreases inflammation by suppressing the migration of polymorphonuclear leukocytes and by reversing capillary permeability. It is a better corticosteroid for intralesional injection as it has better local potency, longer duration of action and lesser systemic absorption.[14] Hyaluronidase is an enzyme which reduces the viscosity of ground substance, thus making the tissues more permeable to injected corticosteroid triamcinolone acetonide. It stimulates hydrolysis of hyaluronic acid, one of the chief ingredients of tissue cement, which offers resistance to diffusion of liquids through tissues. It facilitates distribution and absorption of locally injected substances. It also promotes resorption of excess fluids and extravasated blood in the tissues.[14]

Daga et al (2017)[13] compared the effectiveness of oral colchicine with intralesional injection of hyaluronidase and injection triamcinolone acetonide in patients with Grade II OSMF and concluded that use of injection hyaluronidase with oral colchicine gave better results in terms of increase in mouth opening and improvement in burning sensation without notable side effects.

Low level laser therapy has a photo-biomodulating effect. Low level laser therapy is also known as photobiomodulation (PBM) or cold therapy. In PBM, the output power ranges from 50 to 500 mW, with a wavelength of 630 to 980 nm. The effect of PBM on the tissue is achieved without raising the temperature. PBM acts on cells through cytochrome C oxidase. Mitochondrial membrane potential increases when LASER is absorbed. This interaction of biochemical and molecular processes causes the reduction in pro-inflammatory cytokines and leads to the anti-inflammatory and analgesic properties of PBM.[15]

KESARI SINGH et al (2017)[16] evaluated the efficacy of Low-Level Laser Therapy (LLLT) in treatment of OSMF and concluded that biostimulation by laser in the treatment of OSMF is a good non-invasive, painless and quick alternative treatment modality for the management of the diseases.

Aparna et al (2023)[17] did comparative evaluation of functional outcomes of LLLT and intralesional steroid injection in OSMF patients. Immediate results with laser therapy are good, but intralesional steroid injections remain more effective in the long-term effect.

CONCLUSION

Based on the mechanism of action of the above drugs and beneficial effect of PBM, an attempt was made to study the outcome of the new protocol combining the Intralesional injections (Hyaluronidase and triamcianolone acetomide) with photobiomodulation and systemic intraoral administration of colchicine.

Despite the good results, we are still unclear what is the exact key element or is it the combination of all therapies for this triumph.

The combination of multiple photoceuticle and pharmaceutical therapy will definitely get good results in the management of Stage 1 and 2 Oral Submucous Fibrosis.

Henceforth, this combination therapy can be used as a standard of care for the management of Oral Submucous Fibrosis.

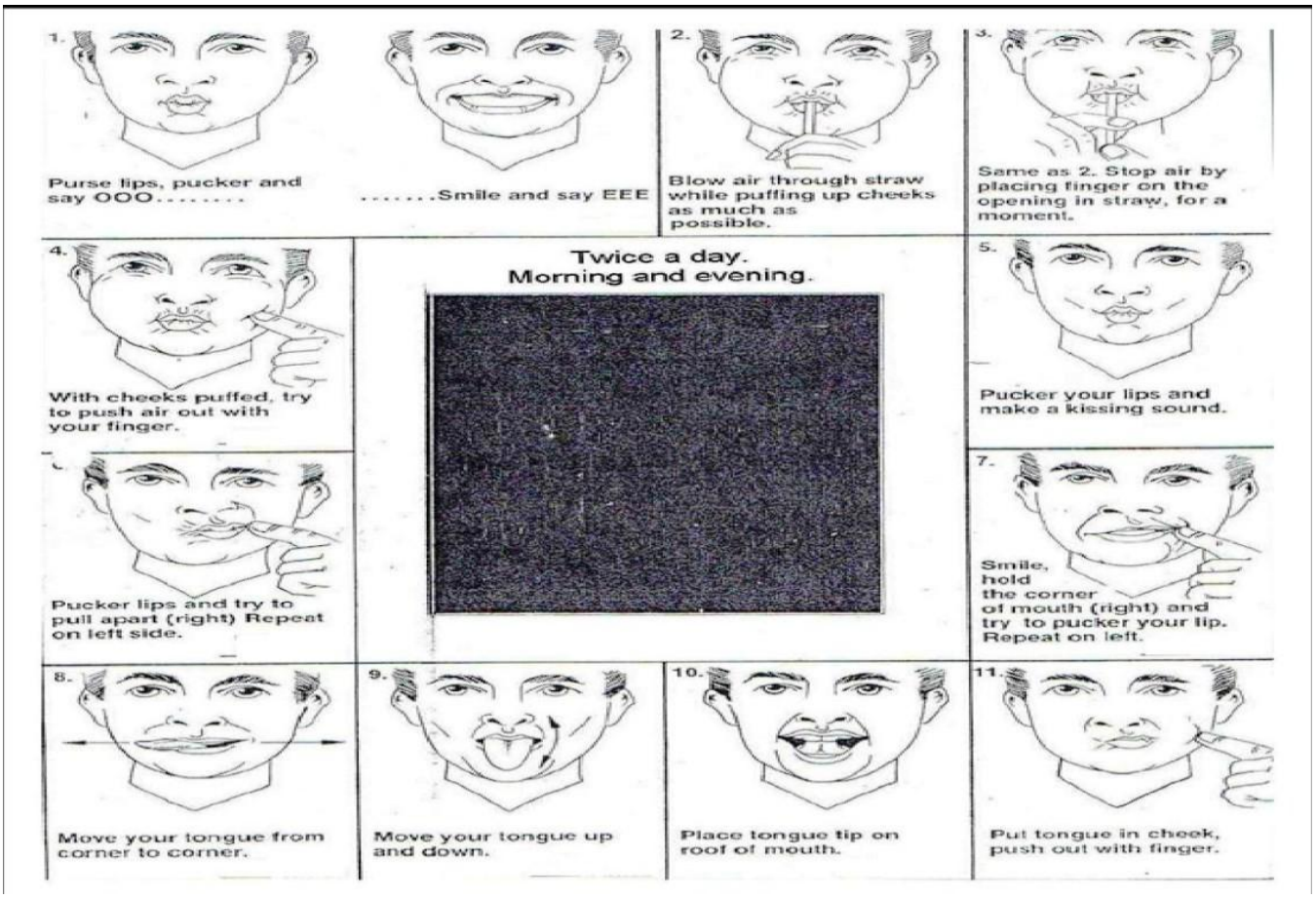

Figure 1. Mouth Exercises

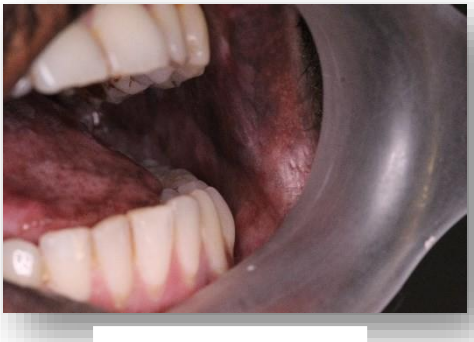

Figure 2 (20mm)

Figure 3

Figure 4

Figure 5

Pre-operative Images

Fig 2: Stiffen left oral mucosa with the appearance of fibrous bands

Fig 3: Stiffen right oral mucosa with the appearance of fibrous bands

Fig 4: Marble stone appearance of palate.

Fig 5: Inter-incisor distance (IID) of 20 mm

Figure 6. Intralesional Injection of 0.1% triamcinolone acetonide and Hyaluronidase 1500 IU

Figure 7. Photobiomodulation (810nm at 100mw delivering a total of 6 joules of energy.)

Figure 8. First week (22mm)

Figure 9. Second week (23mm)

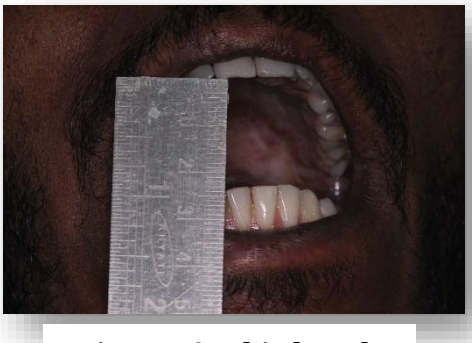

Figure 10. Third week (25mm)

Figure 11. Fourth week (27mm)

Figure 12. Fifth week (28mm)

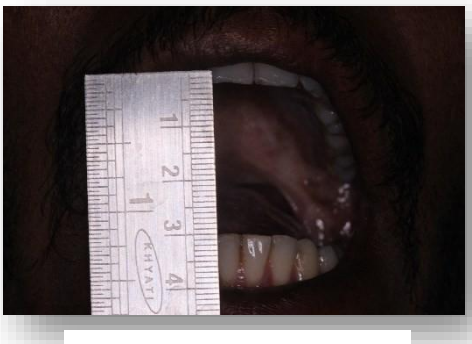

Figure 13. Sixth week (30mm)

Post-operative Images showing gradual increase in inter-incisal distance.

Figure 11. Right buccal mucosa

Figure 12. Left buccal mucosa

Post-operative Images showing pink and soften oral mucosa.

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