



MANAGEMENT OF ORAL SUBMUCOUS FIBROSIS BY TWO DIFFERENT REGIMENS

Shubahshree M¹. Nath, Anilgovind Rao Ghom², Savita Ghom², Ajit Mishra², Arpan Aash¹, Akhil Dwivedi¹


¹Postgraduate student, Department of Oral Medicine and Radiology, Maitri College of Dentistry & Research Centre, Anjora, Durg, CG.

²Professor, Department of Oral Medicine & Radiology, Maitri College of Dentistry & Research Centre, Anjora, Durg, CG.

ABSTRACT

Oral submucous fibrosis is a precancerous condition of the oral mucosa. It also causes chronic inflammation and progressive fibrosis. Here in this study, we had taken 20 patients and randomly divided them into two groups, Group A treated with *Calendula officinalis* extract gel 2mg twice daily for 12 weeks and Group B treated with Triamcinolone acetonide(10mg/ml) + Hyaluronidase (1500 IU) at 1-week interval for 3 months. Treatment modalities depends upon two criteria's: Burning sensation and Mouth opening. An unpaired t-test was used to compare the pre and post-treatment burning sensation and mouth opening. P<0.001 is highly significant. Triamcinolone acetonide shows a significant result in the reduction of mouth opening followed by *Calendula officinalis*. *Calendula officinalis* topical application may need longevity to attain the result. As per our knowledge, none of the studies have been done on *Calendula officinalis* for mouth-opening improvement in oral submucous fibrosis. In our study, it was observed that *Calendula officinalis* was found to be the best non-invasive, safe and cost-effective therapy for mouth opening in Grade II OSMF patients. In burning sensation, *Calendula officinalis* shows 100% results in the reduction of burning sensation compared to Triamcinolone acetonide shows 70% approx. Patients need not be worried about recurrent visits, they can use it by themselves (*Calendula officinalis* extract gel). In the current clinical evidence, *Calendula officinalis* shows a significant result in the management of oral submucous fibrosis, further study on *Calendula officinalis* may enlighten the facts to speak for themselves.

Key words:- OSMF- Oral submucous fibrosis, I.P.- Indian pharmaceutical, IU- International unit, W/V- Weight/ volume.

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INTRODUCTION

Oral submucous fibrosis (OSMF) is a precancerous condition with chronic inflammation and progressive fibrosis of the submucosa. The rapid increase of the disease activity is due to the popularity of commercially prepared areca nut preparations, and increased uptake of

this habit by young people. [1] The prevalence of OSMF in India has been estimated to range from 0.2–2.3% in males and 1.2–4.6% in females, with a broad age range from 11 to 60 years. This malignant transformation rate was reported 7%-13%. [2] Clinical features of oral submucous fibrosis include reduced mouth opening, shrunken uvula, blanching and leathery texture of oral mucosa, burning sensation on spicy food. [2]

Corresponding Author
Shubahshree M

Email: - drshubhashreem@gmail.com

Many studies have been conducted on the treatment modalities of oral submucous fibrosis. Recently Dr. Jeevitha Gauthaman *et al*, explained the increased side effects in conventional medicines have navigated researchers towards herbal medicinal products and also prevent the development of resistant microorganisms and opportunistic infections.^[3]

In oral care, plant and plant-derived products have been used to reduce inflammation and infection and aid in the healing of premalignant conditions most commonly used is Spirulina in oral submucous fibrosis.^[3] Pharmacological studies have confirmed that *C. Officinalis* exhibit antimicrobial, anti-inflammatory, immunomodulatory antioxidant, wound healing, antiviral, and anti-tumoral properties.^[4] So as per the prevalence of OSMF and its increased malignant potential, we took this premalignant condition for our study and *Calendula officinalis* as our treatment modality.

MATERIALS AND METHODS

Twenty patients of Grade- II OSMF were taken for this study, with treatment modality based on (1) Mouth opening and (2) Burning sensation. They were made aware of their condition, its cause, and its malignant potential. All patients underwent informed consent, translated into two local languages, Chhattisgarhi and Hindi. This comparative study was done in the OPD of our college. We compare the effectiveness of *Calendula officinalis* extract gel with a noble treatment modality triamcinolone acetonide + hyaluronidase. The patients were randomly divided into two groups, Group A and Group B. Group A patients were given 2mg of *Calendula officinalis* extract gel for topical application in the region of the fibrous band along with physiotherapy. Group B patients were given a combined injection of triamcinolone acetonide injection I.P. 10mg/ml (kenacort) and Hyaluronidase injection I.P.(Ovine) 1500IU (Hynidase) intralesional. The interincisal mouth opening was measured by Vernier caliper and the burning sensation was measured by Yes or

NO scale.^[5] *Calendula officinalis* of the family Asteraceae were collected from a local vendor during the winter season. Flowers were authenticated by the trained and experienced faculty of Apollo college. other chemicals such as Hydroxymethyl propyl cellulose, methylparaben, and propylparaben used in the formulations were procured from the local dealers.

Per gram of *Calendula officinalis* gel contained^[6]:

1. Compound extract- 2 mg by weight
2. Gelling agent-hydroxy propyl cellulose (5% w/v)
3. Preservative -methylparaben (0.1% w/v), propylparaben (0.01% w/v)
4. Humectant- glycerine (5% w/v)
5. Solvent for menthol-ethanol (2 drops)
6. Sweetening agent-xylitol (1% w/v)
7. Flavouring agent- menthol (0.05% w/v)

We prepare the *Calendula officinalis* extract gel by the help of Apollo pharmacy college near to our college.

RESULTS

After 1 month the mouth opening improved by using *Calendula officinalis* extract gel was 3.7 mm whereas in the case of Triamcinolone acetonide and Hyaluronidase combination Inj improved it approx. 5.7 mm which is statistically significant. P value is 0.000(P<0.001). It suggests mouth opening is better improved by steroid combination followed by *Calendula officinalis* extract, in which long duration of topical application is required for improvement in mouth opening. After 1 month the burning sensation reduced by using *Calendula officinalis* extract gel was 100% whereas in case of Triamcinolone acetonide and Hyaluronidase combination inj reduced it to 100% by 47 days, which is statistically significant. P value is 0.0009(P<0.001). It suggests burning sensation was better reduced by *Calendula officinalis* extract gel followed by triamcinolone acetonide + Hyaluronidase Inj combination, in which long duration of topical application is needed.

Table 1: Comparison of improvement in mouth opening in OSMF patients of Group A (*Calendula officinalis* extract gel) and Group B (Triamcinolone acetonide + Hyaluronidase Inj) after applying unpaired “t” test on the application of medications.

S.No	Study groups	Comparison of improvement in mouth opening in mm (After application of medicaments) (Mean± S.D.)	t value	p value
1	Group A (<i>Calendula officinalis</i> extract gel)	3.7± 0.82	-4.7	0.000 (P<0.01) Very Highly significant
2	Group B (Triamcinolone acetonide + Hyaluronidase Inj)	5.7± 1.05		

Table:2 Comparison of improvement in mouth opening in OSMF patients of Group A (*Calendula officinalis* extract gel) and Group B (Triamcinolone acetonide + Hyaluronidase Inj) after applying unpaired “t” test on application of medications.

S.No	Study groups	Comparison of elimination of burning sensation in days (After application of medicaments) (Mean+ S.D.)	t value	p value
1	Group A (<i>Calendula officinalis</i> extract gel)	33.2± 5.95	-4.3	0.0009 (P<0.001) Very Highly significant
2	Group B (Triamcinolone acetonide + Hyaluronidase Inj)	46.9± 8.11		

[Series 1- CALENDULA OFFICINALIS EXTRACT GEL; Series 2-TRIAMCINOLONE ACETONIDE+HYALURONIDASE] [GRAPHICAL REPRESENTATION OF MOUTH OPENING IMPROVEMENT]

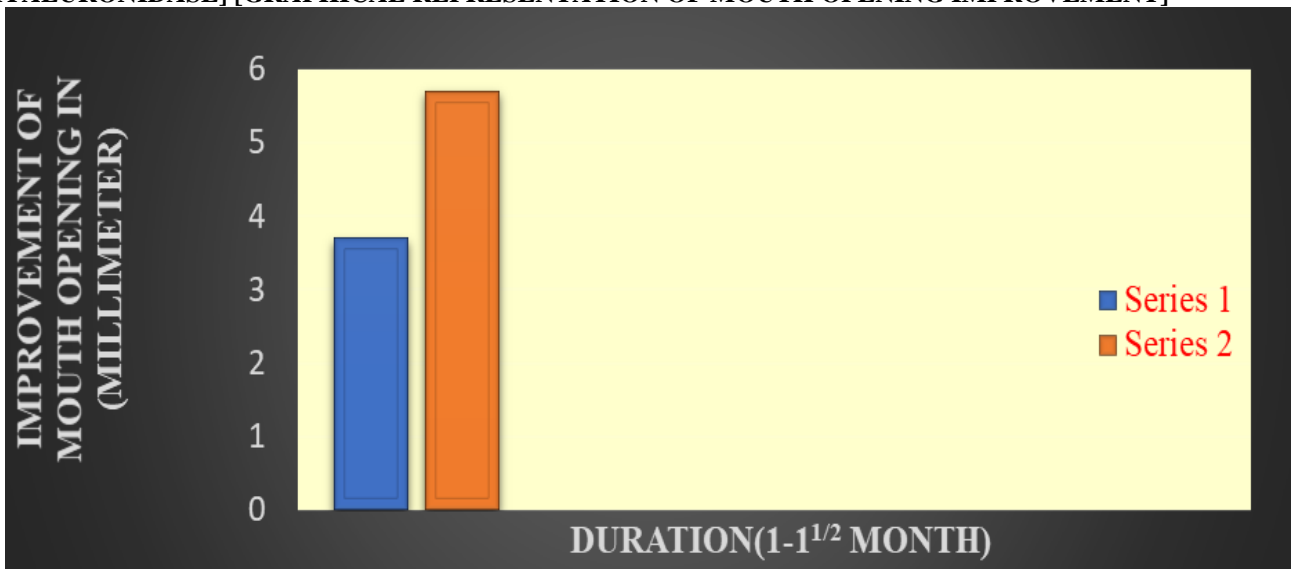
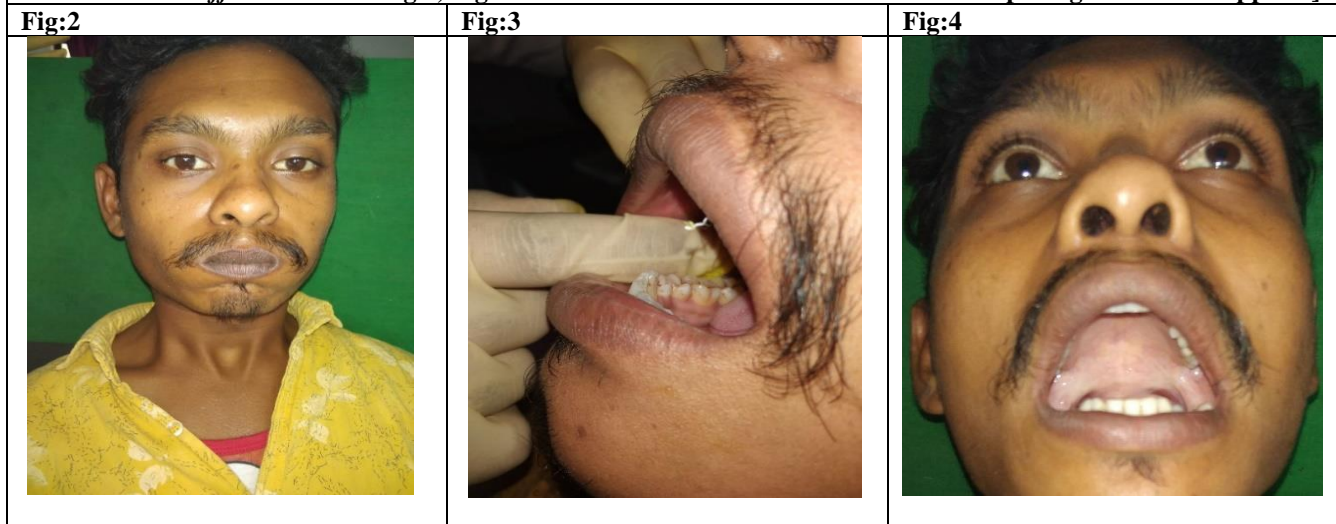
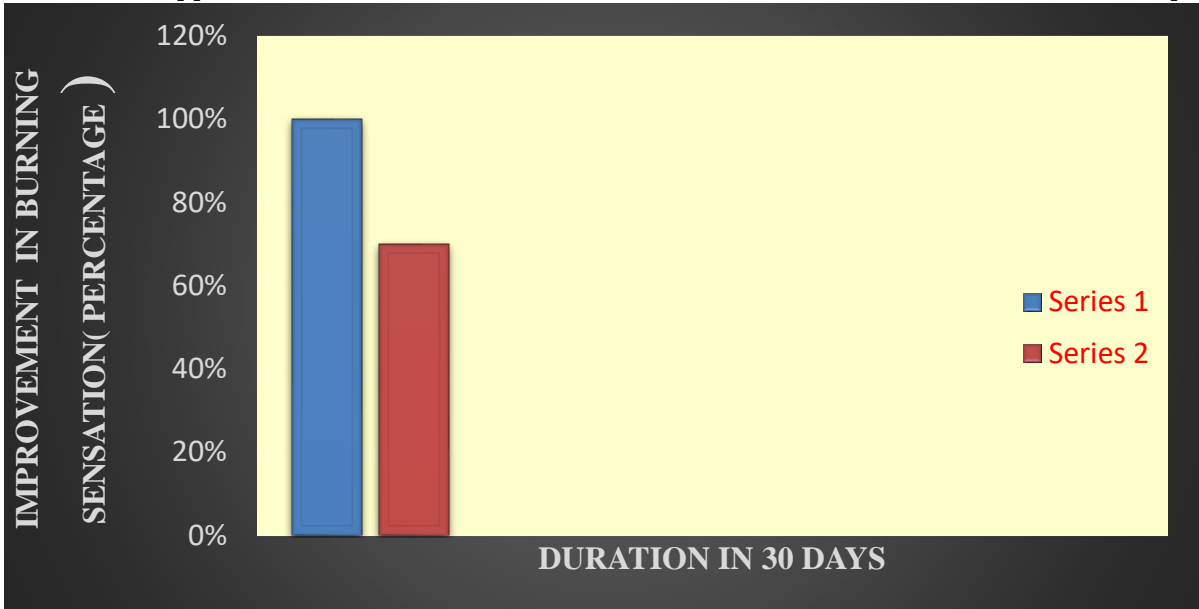


Fig:2 Grade II oral submucous fibrosis patient (first patient); Fig:3 Patient with 30 mm of mouth opening, treated with *Calendula officinalis* extract gel; Fig:4 After 2 months the Post treatment mouth opening was 33 mm approx.]



[Series 1- *CALENDULA OFFICINALIS* EXTRACT GEL; Series 2-TRIAMCINOLONE ACETONIDE+HYALURONIDASE] [GRAPHICAL REPRESENTATION OF BURNING SENSATION IMPROVEMENT]



[Fig:5 Grade II oral submucous fibrosis patient (Second patient); Fig: 6 Patient with 27 mm of mouth opening, treated with Inj of Triamcinolone acetamide (10mg) + Hyaluronidase(1500IU); Fig: 7 After 2 months the Post treatment mouth opening was 35 mm approximately]



Discussion

Oral Submucous Fibrosis (OSMF) is a chronic disease of insidious onset affecting the oral mucosa with progressive involvement of the pharynx and esophagus. Patients frequently present with pain, intolerance to hot & spicy food, and reduced mouth opening. Areca nut contains nitrosamines and nitrite strongly develops this condition. Chilies and spices were also one of the predisposing factors of OSMF. [1] Various treatment modalities have been proposed for OSMF. On a broader scale, two basic approaches are known for the management of OSMF, surgical and conservative treatment. Surgical methods are reserved for severe trismus. It involves fibrotomy to release the fibrotic areas, but it leads to further scarring and fibrosis. In-band excision, different flaps have been used as interpositional

tissue like a buccal fat pad, tongue flaps, palatal island flaps, nasolabial flaps, temporalis fascia flaps, or free tissue transfer. [7] Conservative treatment includes physiotherapy and medical management. The basic aim of physiotherapy is to induce tissue remodeling to enhance the stretching of the mucosa, and splint increases the mouth opening. Medical treatment comprises iron and vitamin supplements like lycopene along with spirulina. Other medicines include intralesional injection of corticosteroids + enzymes for proteolysis (hyaluronidase), and aqueous extract of healthy human placenta. [7] In the present study, 20 (Oral submucous fibrosis) patients were selected and divided into two groups that are Group A treated with *Calendula officinalis*, and Group B treated with Triamcinolone Acetonide+ Hyaluronidase for 2 months. Mouth opening was measured by Vernier caliper

in pre-treatment and post-treatment visits. The burning sensation was measured by Yes/ No scale. In 2008 John Dawes et al. showed this scale in their research article. [5] In the present study, the improvement in mouth opening for Group A was 3.7 mm. As per our knowledge, there was no study conducted on *Calendula officinalis* for the treatment of oral submucous fibrosis. We took reference from these studies conducted by G. K. Shakunthala et al (2017) [8], in which they found that reduced antioxidant status in their patients was due to excessive utilization of antioxidants to scavenge the free radicals, generated during the pathogenesis of the disease. Another study by Jurga Bernatoniene et al (2010) [9], in which they found that ROS causes lipid peroxidation of the skin and reduces natural barrier function. Topical antioxidants may protect the skin from burning and laceration. Among all *Calendula* constitute mainly flavonoids and carotenoids so highly effective in ROS-caused damage. This finding should assist us in our study. The improvement in mouth opening for Group B was 5.7 mm. The study conducted by Sudhir M Naik et al (2012), Anuradha Pai et al. (2021), and Kapil Kumar et al (2019), Mohd Aftab et al have a similar result to our study. [10] [11] [12] [13]

After 1 month the burning sensation reduced by using *Calendula officinalis* extract gel was 100% whereas in the case of Triamcinolone acetonide and Hyaluronidase combination inj reduced it to 100% by 47 days, so longevity is needed.

As we mentioned above that there was no study conducted on *Calendula officinalis* however Preethi KT et al (2009) [14] showed the effect of *Calendula officinalis* flower extracts on thermal burns. They concluded that *Calendula* extract may be activated by modifying the activities of proinflammatory cytokines and inhibiting the cyclooxygenase-2 enzyme, increasing the burn injury's healing potential and relieving the pain. We conjugate these mechanisms in our study process. Preethi K et al. (2009), Diva silva et. al (2021), and Khulood M. Alsaraf et.al (2019) studied the efficient activity of *Calendula officinalis* in the burn. [14] [15] [16]

Triamcinolone acetonide and Hyaluronidase combination inj is less prevalent in the reduction of burning sensation compared to topical antioxidants like *Calendula officinalis* extract gel. A similar result was appreciated by T. A. Deepak et al (2021) [17] in their study.

CONCLUSION

Oral submucous fibrosis is an insidious chronic, potentially malignant disorder. The management of OSMF includes medical, surgical, and physiotherapeutic modalities. A study conducted by Dr. Jeevitha Gauthaman et al, explained the increase in adverse effects in conventional medicines has navigated researchers toward safe herbal medicinal products and also prevent the development of resistant microorganisms and opportunistic infections. After gathering recent information about phytochemical constituents and properties regarding the treatment of oral submucous fibrosis we explore a renovation in the field of medicine, as we prepared *Calendula officinalis* extract gel. Here we conducted a study by taking an Intralesional injection of Triamcinolone acetonide+ Hyaluronidase, and *Calendula officinalis* extract gel, a non-invasive method of treating Grade II OSMF patients for 3 months. As per the study conducted till now, it has been proved that *C. Officinalis* has antimicrobial, anti-inflammatory, immunomodulatory, antioxidant, wound healing, antiviral, and anti-tumoral properties. Steroids have anti-inflammatory properties. Cytokines and growth factors produced by inflammation can promote fibrosis by inducing the proliferation of fibroblast, sub-regulating collagen synthesis, and down-regulate collagenase production. Steroids decrease inflammation by suppressing the migration of polymorphonuclear leukocytes and reversing capillary permeability. Corticosteroid in intralesional injection has better local potency, longer duration of action, and lesser systemic absorption. Hyaluronidase degrades the fibrous matrix promoting lysis of the fibrinous coagulum and activating specific plasmatic mechanism of Steroid. We concluded that steroid is highly effective in improving mouth opening although *Calendula officinalis* topical application may need longevity to attain the result. In burning sensation, the best-suited treatment modality is *Calendula officinalis*. *Calendula officinalis* is non-invasive and patients need not be worried about recurrent visits they can use it by themselves. Along with physiotherapy, it has a good prognosis in the inter-incisal mouth opening and burning sensation along with physiotherapy. We also emphasized that further studies on larger sample size is required to compare these groups (Triamcinolone acetonide + Hyaluronidase, *Calendula officinalis*).

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