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Research Article

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EVALUATION OF EFFICACY OF CURCUMIN AND PHYSIOTHERAPY IN THE MANAGEMENT OF ORAL SUBMUCOUS FIBROSIS - A CLINICAL STUDY

^{*1}Dr. Yamuna Rani and ²Dr. Anuradha Pai

¹Post Graguate Student, Department of Oral Medicine & Radiology, The Oxford Dental College, Bangalore.

²Professor & Head of the Department, Department of Oral Medicine & Radiology, The Oxford Dental College, Bangalore.

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*Corresponding Author Dr. Yamuna Rani Post Graguate Student, Department of Oral Medicine & Radiology, The Oxford Dental College, Bangalore.

ABSTRACT

Aim: To clinically determine and Compare the efficacy of curcumin gel and triamcinolone acetonide gel with physiotherapy in the management of oral submucous fibrosis. **Materials and Methods:** 60 patients of OSMF were randomly divided into 2 groups (Group I and Group II). The group 1patients was given curcumin gel and were asked to apply the gel three times a day on each side of the affected site, by using a sterile cotton guaze or with clean finger tips. The group 2 was given triamcinolone acetonide gel and were asked to apply the gel three times a day on each side of the affected site, by using a sterile cotton guaze or with clean finger tips. The group 2 was given triamcinolone acetonide gel and were asked to apply the gel three times a day on each side of the affected site, by using a sterile cotton gauze or with clean finger tips. The results were subjected to statistical analysis. Ethical committee clearance reference number:

TODC/221/ECAL/2020-21. Results: Group I showed better

improvement in burning sensation and increase in inter incisal mouth opening when compared to Group II. Both the groups showed a statistically significant reduction in cheek flexibility and tongue protrusion at the end of study period (p<0.001). **Conclusion:** In OSMF patients the clinical response to Curcumin gel was comparable to triamcinolone acetonide gel. Hence, the study concludes that Curcumin can be an alternative, safe and effective treatment regime in the management of OSMF. Long term follow up studies with larger sample size are recommended.

KEYWORDS: OSMF, oral submucous fibrosis, Curcumin, Turmeric, Triamcinolone acetonide and Physiotherapy.

INTRODUCTION

Oral submucous fibrosis (OSMF) has been described 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 a juxtaepithelial inflammatory reaction followed by a fibro-elastic change of the lamina propria, with epithelial atrophy leading to stiffness of the oral mucosa and causing trismus and inability to eat."^[1] Oral submucous fibrosis is a debilitating condition causing an overall reduction in the quality of life due to its ability to cause problems with speech, swallowing, opening of the mouth as well as the chances of developing into a malignant lesion.^[2]

The etiopathogenesis of OSMF is complex and incompletely understood. Oral Submucous Fibrosis is a potentially malignant disorder attributed to areca nut (betel nut) chewing. The other proposed etiological factors include excessive chilly consumption, vitamin B and iron deficiency, autoimmunity, genetic and environmental factors.^[3] OSMF is the first demonstrated oral disease which is related with sustained effect by the irritants on the oral mucosa. Numerous studies that clarified its etiopathogenesis have focused on the extracellular matrix (ECM) with increased synthesis of subepithelial collagen and decreased collagen degradation. Though the etiopathogenesis of OSMF is still not completely clear.^[4] The increasing trend of consuming areca nut with tobacco has greatly increased OSMF frequency.^[5] The use of areca nut is thought to be the most important causative factor.

Areca nut consists of alkaloids such as arecaidine, arecoline, and guvacoline apart from flavonoids, tannins, catechin, and copper. The alkaloids stimulate the fibroblasts to produce more collagen.^[6] while its structure is stabilized by catechin and tannins. The increased crosslinkage of collagen results from upregulation of the copper dependent enzyme lysyl oxidase. Documented evidence favors areca nut as the main etiological agent owing to cytotoxic, apoptotic and proliferative effects. The cytotoxic effects, in addition to the release of free radical induced mutations by areca nut, induces genotypic & phenotypic alterations, a key point in the pathogenesis of OSMF.^[3] Studies have also found that chewing dried areca nuts are more pathogenic and carcinogenic than chewing fresh areca nuts, and the extremely harmful ingredients in areca nuts play a vital role in the occurrence of oral mucosal diseases and oral cancer.^[4]

OSMF occurs at any age but is most commonly seen in adolescents and adults especially between 16 and 35 years. It is predominantly seen in Southeast Asia and Indian subcontinent with few cases reported from South Africa, Greece and United Kingdom.12 It may be associated with oral leukoplakia and other potentially malignant disorders or with oral malignancy. The prevalence rate of OSMF in India is about 0.2 to 0.5%. The reasons for the rapid increase in the prevalence is due to an upsurge in the popularity of commercially prepared arecanut and tobacco preparations-gutkha, pan masala, mawa, flavored supari, etc.^[7] There has also been a steady increase in stress that a human has to cope. In this scenario, people fall for habits such as gutkha, tobacco, and betel nut chewing are of great relief. They not only are addictive but also can cause debilitating irreversible damage to the oral cavity, one of which is the oral submucous fibrosis (OSMF).^[2]

A wide range of treatment modalities have been proposed for OSMF but none have proved curative or reduced the morbidity significantly. Hence, the search for effective treatment modality still continues.^[8] Various medical interventional therapies are reported in literature ranging from nutritional supplements, antioxidants, immunomodulators, biogenic stimulators, enzymes, fibrinolytic agents, and vasodilators in systemic, topical, and intralesional forms.Advanced lesions are treated surgically.^[5]

Curcumin (diferuloylmethane) is a polyphenol compound isolated from ground rhizomes of the plant (Curcuma longa) L. (Zingiberaceae) found in South Asia.^[9] Curcumin is the active ingredient of turmeric responsible for its yellow color and several important pharmacological properties.^[10] A large number of studies have revealed that Curcumin has wide therapeutic actions such as antiinflammatory, antioxidant and anticancer properties. Curcumin have been studied for treatment of OSMF.^[11] All these properties of curcumin suggest the possibilities of its usage in the management of OSMF.

Hence present study was designed to evaluate the efficacy of curcumin gel with oral physiotherapy versus triamcinolone acetate 0.5% with oral physiotherapy in the management of OSMF.

MATERIALS AND METHODS

The present clinical study was done in the Department Of Oral Medicine and Radiology, The Oxford Dental College, Bangalore. Prior to conducting the study, ethical clearance was obtained from the ethical board of The Oxford Dental College. Informed consent from the

patients were taken. Detailed case history and clinical findings was recorded on a proforma. The study participants were divided into two groups.

Clinically diagnosed OSMF patient, healthy individuals without any systemic diseases, patients who were ready to quit the habit and accept regular follow -up protocol, and patients willing to register for the study with written consent were included in the study. Patients were given freedom to withdraw from study anytime during the course of the study.

Patients presenting with co existing malignancy / white lesions, patients with known allergy to drugs, patients who are previously treated for OSMF, patients with any systemic disease, patients who were uncooperative were excluded from the study.

The study population consisting of 60 patients were divided randomly into two groups, each group consisting of 30 patients each.

- Group I : Curcumin :- Curenext Oral Gel- Curcuma longa extract 10mg, Erythrosine and Titanium Dioxide IP (Manufactured by Abbott Healthcare Pvt.Ltd).
- Group II: Trioplast Gel -Triamcinolone Acetonide IP 0.1%W/W (Manufactured by ICPA Health Products Limited)

The clinical and functional staging of OSMF were done based on Chandramani More et al.(2011)^[7,51] classification and were classified into Clinical staging and Functional staging.

Clinical staging

- 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) as follows.
- a. Any one of the above stage along with other potentially malignant disorders, e.g. oral leukoplakia, oral erythroplakia, etc.^[44]
- ▶ b. Any one of the above stage along with oral carcinoma.^[44,51]

Functional staging

M1: Interincisal mouth opening up to or greater than 35 mm.

M2: Interincisal mouth opening between 25 and 35 mm.

M3: Interincisal mouth opening between 15 and 25 mm.

M4: Interincisal mouth opening less than 15 mm.

After obtaining informed consent, detailed case history was recorded. The following parameters were noted.

The patients were comfortably seated on a conventional dental chair. Detailed history with special emphasis on type, frequency and duration of habit (areca nut, gutkha or combination of both), whether they swallowed the product or spitted it out were noted. Clinical examination was done through the assessment of subjective symptoms like burning sensation, objective signs like interincisal distance (IID), tongue protrusion and cheek flexibility.

Intensity of burning sensation was recorded using a Visual Analogue Scale, (VAS) of 0-10, where 0 indicated no burning sensation and 10 indicated the worst possible burning sensation. The interincisal distance was measured using a OSMF scale from the mesioincisal angle of upper central incisor to the mesioincisal angle of lower central incisor and recorded in millimeters. Cheek flexibility was measured according to the method by More et al 2011.^[5,7] in millimeters, from the maxillary incisal midline to the cheek retractor during retraction. Tongue protrusion was assessed from normal mesioincisal angle of upper central incisor to the tip of tongue when maximally extended with mouth wide open. History and clinical examination data were entered in the pre prepared proforma. All 60 OSMF patients were divided into two groups: Group 1 - 30 patients diagnosed with OSMF were given oral application of curcumin gel and patient were instructed to do the oral physiotherapy excercises for a period of 3 months. Group 2 - 30 patients diagnosed with OSMF were given oral application of triamcinolone acetonide gel and patient were instructed to do the oral physiotherapy excercises for a period of 3 months. Patients were encouraged through education, counseling, and advocacy to discontinue the habit and were assisted for habit cessation at every visit till the end of 3months. The exercise like tongue blade, china ball excercise, blowing the mouth and tongue protrusion exercises was advised to do daily for five times for 3 months. Patients were recalled for 3 months in the time intervals by baseline, 15th day, 1st, 2nd and 3rd month to check for the mouth opening, Cheek flexibility, tongue protrusion and to asses the burning sensation.

Collected data were analyzed by using Statistical Package for Social Sciences [SPSS] for Windows Version 22.0 Released 2013. Armonk, NY: IBM Corp., was used to perform statistical analyses.

Descriptive Statistics

Descriptive analysis of all the explanatory and outcome parameters were done using frequency and proportions for categorical variables, whereas in Mean & SD for continuous variables.

Inferential Statistics

Mann Whitney test was used to compare the mean age and values of different study parameters between 2 groups at different time intervals.

Chi Square Test was used to compare the gender distribution and OSMF staging between 2 groups.

Friedman's test followed by Wilcoxon Signed Rank Post hoc Test was used to compare the mean values of study parameters between different time intervals in each group.

The level of significance was set at P < 0.05.

Ethical committee clearance reference number :TODC/221/ECAL/2020-21

PHOTOS

Group I: Curcumin.



PHOTOGRAPH-1 :(a) Measurement of inter incisal distance and tongue protrusion in Group I at baseline



PHOTOGRAPH-1:(b) Measurement of inter incisal distance and tongue protrusion in Group I at 90 days.

GROUP II: TRIAMCINOLONE ACETONIDE



PHOTOGRAPH-2:(a) Measurement of inter incisal distance and tongue protrusion in Group II at baseline.



PHOTOGRAPH-2:(b) Measurement of inter incisal distance and tongue protrusion in Group II at 90 days.

Age and gender distribution among 2 groups									
Variable	Category	Gro	oup 1	Gro	n voluo				
		Mean	SD	Mean	SD	p-value			
Age	Mean	33.47	8.35	36.67	10.19	0.22 ^a			
	Range	23	- 56	23	0.23				
		n	%	n	%				
Sex	Males	26	86.7%	24	80.0%	0.40 ^b			
	Females	4	13.3%	6	20.0%	0.49			

TABLES



Graph 1a

Table 2.

Comparison of mean Burning Sensation scores b/w diff. time intervals in each group using Friedman's test								
Group	Time	N	Mean	SD	Min	Max	p-value	
	Baseline	26	6.69	1.35	5	9		
	15 Days	26	5.42	1.39	3	8		
Group 1	30 Days	26	3.92	1.13	2	6	<0.001*	
-	60 Days	26	2.81	0.80	1	4		
	90 Days	26	1.77	0.77	0	3		
Group 2	Baseline	26	6.08	1.50	4	10	<0.001*	
	15 Days	26	5.54	1.36	4	9		
	30 Days	26	4.92	1.41	3	9		
	60 Days	26	4.50	1.48	2	8]	
	90 Days	26	4.31	1.46	1	8]	

Table 3.

Comparison of mean Mouth Opening (in mm) b/w diff. time intervals in each group using Friedman's test

Group	Time	Ν	Mean	SD	Min	Max	p-value
Group 1	Baseline	26	32.88	4.62	26	45	
	15 Days	26	35.38	4.52	27	47	
	30 Days	26	37.92	4.22	30	49	< 0.001*
	60 Days	26	40.19	4.09	33	51	
	90 Days	26	42.42	3.75	35	52	
Group 2	Baseline	26	32.46	4.34	25	38	
	15 Days	26	34.19	4.20	27	39	
	30 Days	26	35.58	3.96	28	40	< 0.001*
	60 Days	26	37.08	3.61	30	41	
	90 Days	26	38.81	3.53	31	44	

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Comparison of mean Cheek Flexibility (in mm) b/w diff. time intervals in each group using Friedman's test								
Group	Time	N	Mean	SD	Min	Max	p-value	
	Baseline	26	20.19	3.60	14	27		
	15 Days	26	21.15	3.45	14	28		
Group 1	30 Days	26	22.69	3.51	15	29	<0.001*	
_	60 Days	26	24.54	3.41	16	30		
	90 Days	26	26.27	3.48	17	32		
	Baseline	26	19.69	3.81	13	26	<0.001*	
	15 Days	26	20.73	3.71	15	26		
Group 2	30 Days	26	21.65	3.67	16	27		
	60 Days	26	22.50	3.69	17	28		
	90 Days	26	23.23	3.81	17	29		

Table 5.

Comparison of mean Tongue Protrusion (in mm) b/w diff. time intervals in each group using Friedman's test								
Group	Time	Ν	Mean	SD	Min	Max	p-value	
Group 1	Baseline	26	49.42	7.52	35	65		
	15 Days	26	52.54	4.89	42	66		
	30 Days	26	54.23	4.62	44	67	<0.001*	
	60 Days	26	56.15	4.10	47	68		
	90 Days	26	58.31	3.61	50	68		
Group 2	Baseline	26	50.31	3.79	40	56		
	15 Days	26	51.35	3.99	41	58		
	30 Days	26	52.27	4.18	41	61	<0.001*	
	60 Days	26	53.15	4.28	42	62]	
	90 Days	26	53.92	4.44	42	63]	

* - Statistically Significant

RESULTS

The study comprised of total 60 OSMF patients within age range of 23 to 56 yrs in Group I and 23 to 64 yrs in Group II. Mean age of subjects in Group I was 33.47 ± 8.35 years whereas in Group II, mean age noted was 36.67 ± 10.19 years. In Group I - 26 (86.7%) subjects were males and 4 were females (13.3%) and Group II - 24 (80.0%) subjects were males and 6 were females (20.0%). Patients of Group I comprised of 13 subjects (43.3%) reported to have stage I and 17 subjects (56.7%) reported to have stage II. In Group II comprised of 16(53.3%) reported to have stage I and 14 subjects (46.7%) reported to have stage II.

Burning sensation

Comparison of mean Burning Sensation scores b/w diff. time intervals in each group

Showed reduction in mean values for burning sensation in each study group between different time intervals were statistically significant. From baseline to 90 days the reduction was 6.69 ± 1.35 to 1.77 ± 0.77 in Group I. Group II also showed significant reduction from 6.08 ± 1.50 to 4.31 ± 1.46 .

Mouth Opening

Comparison of mean Inter Incisal Distance (in mm) between different time intervals in each study group

Mean value increase in inter incisal distance was 32.88 ± 4.62 mm to 37.92 ± 4.22 mm in Group I and 32.46 ± 4.34 mm to 35.58 ± 3.96 mm in Group II from baseline to 30 days. Group II showed improvement of 35.58 ± 3.96 mm to 37.08 ± 3.61 mm from 30 days to 60 days whereas Group I showed 37.92 ± 4.22 mm to 40.19 ± 4.09 mm. An increase of 42.42 ± 3.75 mm and 38.81 ± 3.53 mm was noted for Group I and Group II respectively at the end of 90 days. The improvement in mean values for inter incisal distance in each study group between different time intervals were statistically significant.

Cheek Flexibility

Comparison of mean Cheek Flexibility (in mm) between different time intervals in each study group

Group I subjects showed improvement of cheek flexibility of 20.83 ± 3.78 mm to 26.27 ± 3.48 mm from baseline to 90 days. In Group II, the improvement of cheek flexibility from baseline to 90 days was 19.87 ± 3.86 mm to 23.23 ± 3.81 mm. Overall Group I and Group II both showed better improvement of cheek flexibility at 60days and 90 days. The increased in mean values for cheek flexibility in each study group between different time intervals were statistically significant.

Tongue Protrusion

Comparison of mean Tongue Protrusion (in mm) between different time intervals in each study group

For tongue protrusion the mean improvement for Group I from baseline to 90 days was 6.69 ± 1.35 mm to 1.77 ± 0.77 mm. In Group II, the mean improvement from baseline to 90 days was 6.08 ± 1.50 mm to 4.31 ± 1.46 . The increased in mean values for tongue protrusion in each study group between different time intervals were statistically significant.

DISCUSSION

Oral submucous fibrosis is a debilitating condition causing an overall reduction in the quality of life due to its ability to cause problems with speech, swallowing, opening of mouth and also the chances of developing into a malignant lesion. In India, the overall prevalence rate of OSMF is estimated to be about 0.2–0.5% and varies from 0.2 to 2.3% in males and 1.2 to 4.57% in females.^[2,13,44] The condition is characterized by a burning sensation of the oral mucosa, ulceration, pain, blanching of oral mucosa, depapillation of tongue, depigmentation of oral mucosa, progressive reduction in mouth opening (MO), and scarring of the mucous membrane. The atrophic mucosa may often ulcerate subsequently leading to malignancy.^[2]

Various medical interventional therapies are reported in literature ranging from nutritional supplements, antioxidants, immunomodulators, biogenic stimulators, enzymes, fibrinolytic agents, and vasodilators in systemic, topical, and intralesional forms.^[5,6,15,16,17,20,22,41,42,56]

Many treatment modalities in current practice for OSMF are circumstantial and most of the studies which tested various therapies lacked good design and planning. Hence, need of a good research and awareness still persists to clinicians as well as patients.^[1] Considering the fact that the disease is widely prevalent in socio-economically backward strata, a costeffective treatment modality must be designed.^[5] The treatment for patients who are unwilling for intralesional injections can be advised to do mouth exercises to increase the mouth opening, tongue protrusion and cheek flexibility.^[26] Physiotherapy Exercise, which has been shown to have a significant influence on the treatment of OSMF, is included in These cost-effective, simple physiotherapy management. are and to maintain.^[33,26,15,35,33,16,27,28,20,56]

Management of OSMF has also been tried by using topical steroid Triamcinolone acetonide, which acts as an immunosuppressant, anti-inflammatory, and antifibrotic agent. Triamcinolone acetonide (TA) is an intermediate-acting steroid commonly used by practitioners in the form of topical gels and intralesional injections.^[42,41,21,22,15,16,20,5,56,45]

Curcumin (diferuloylmethane), an orange-yellow component of turmeric is a polyphenol natural product isolated from the rhizome of the plant Curcuma longa. Its effects are diverse and appear to involve the regulation of various molecular targets. Thus, due to its efficacy and regulation of multiple targets, as well as its safety for human use, curcumin has received considerable interest as a potential therapeutic agent for the prevention and treatment of various potentially malignant disorders, malignant diseases, and inflammatory illnesses.^[8] As it is nontoxic and has a variety of therapeutic properties including antioxidant, anti-inflammatory, antiseptic activity, anticarcinogenic activity, chemopreventive, chemotherapeutic activity, anti-tumour, antiviral, antibacterial, antifungal properties and antiplatelet acticvity.^[9,1,3,5,13,11,56]

A study was done in 2020 by Lanjekar AB et al.^[2] to compare the efficacy of topical curcumin gel with triamcinolone-hyaluronidase gel individually and in combination for the treatment of Oral Submucous Fibrosis. In 2020 Ekta ingle.^[5] conducted A systematic review and meta-analysis on Turmeric in the management of Oral Submucous Fibrosis.All parameters such as burning sensation, inter incisal distance and tongue protrusion showed improvement in other studies, except cheek flexibility. Till now very few studies are done in which Oral Physiotherapy was considered in the management of OSMF. The present study was performed to evaluate the efficacy of curcumin in the improvement of burning sensation, inter incisal distance, tongue protrusion and cheek flexibility with oral physiotherapy in OSMF patients. The present study also compared the effect of curcumin with a more widely used treatment modality for OSMF that is topical corticosteroids, triamcinolone acetonide with oral physiotherapy.

In the present study, male predominance was noted in both the groups and most of the study subjects were in the age group of third decade which was similar to the studies conducted by Arpita Rai et al.^[10], Vishwambhar singh et al.^[20], Chtistopherb V. Shinde et al.^[22] Male predominance in this study can be due to easy accessibility for males to use areca nut and its product.

In present study, stage II OSMF was more in group I and stage I OSMF was more in group II. In the advanced stage of OSMF(stage III), a fibrous band that restricts mouth opening (trismus) is characteristic. It causes further problems in oral hygiene, speech, mastication, and possibly swallowing. Development of fibrous bands in the lip leads to thickening and rubbery appearance. It becomes difficult to retract or evert the lips, which transform into an elliptical shape. In more advanced stage of OSMF(stageIII) the efficacy of pharmacological treatment is limited. Patients may benefit from surgery or laser surgery in such situations.⁵⁹Hence stage III was not included in our study.

The present study showed improvements in burning sensation, Comparison of mean Burning Sensation scores b/w diff. time intervals in each group was statistically significant at (p-value <0.001). With Multiple comparison of mean difference at different time intervals in Burning Sensation scores b/w each group (p-value <0.001) Statistically Significant. Hence this study showed that Curcumin is more effective in reducing burning sensation. These findings are in accordance with study reported by Das DA *et al.*^[29] in 2010, Syed Arshiya Ara et al.^[8] in 2017, Jain et al.^[45] in 2016 and Lanjekar et al in 2020.^[45]

In the present study, a statistically significant (P- value of 0.04, 0.004 and <0.001) improvement in inter incisal distance was observed for both the groups at 30 days, 60 days and 90 days respectively but group I showed better improvement in mouth opening. Monu Yadav et al.^[3] in 2014 reported that the patients treated with curcumin with intralesional steroid showed the mean increase in inter incisal distance was 3.13 mm and 1.25 mm respectively in groups I & II. The inter incisal distance improved in both the groups, with signifificant results at the end of first month.^[3] Hazarey *et al.*, in their study reported 5.93 (±2.37) mm increase in mouth opening for test group(Curcumin) compared to 2.66 (±1.76) mm of the control group.^[8]

Comparison of mean Mouth Opening b/w diff. time intervals in each group was statistically significant (p <0.001). Multiple comparison of mean difference in Mouth Opening b/w time intervals in each group was statistically significant. This study showed that Curcumin is more effective in improving mouth opening.These findings are similar in concordance with study reported by Yadav M et al.^[9] Agarwal N et al.^[9] and Hazarey et al.^[9]

In the present study, improvement in cheek flexibility was statistically significant. Comparison of mean Cheek Flexibility b/w diff. time intervals in each group was statistically significant at<0.001. These findings are similar in concordance with study reported by Kuttan et al.^[8], Li et al.^[8]

Group I and Group II showed statistically significant increase in tongue protusion at 60 days and 90 days. A gradual increase was noted in both the groups at each visit. Das DA *et al.*^[29,10] in 2010, obtained better improvement in tongue protrusion in turmeric oil group than systemic application of turmeric. While study done by Monu Yadav *et al.*^[3,10] found no significant improvement of tongue protrusion in turmix group, whereas it was maximal at the

end of 1st month with conventional therapy (steroid injection group). Darakhshan Rizvi et al.^[6] found significant improvement in tongue protrusion with both tulsi and curcumin.

In the present study, improvement in tongue protrusion was statistically significant. Comparison of mean Tongue Protrusion (in mm) b/w diff. time intervals in each group was statistically significant at <0.001. This study showed that Curcumin is more effective improvement in tongue protrusion. These findings are similar in concordance with study reported by Arpita Rai et al.^[10], Kuttan et al.^[8], Li et al.^[8], Yadav M et al.^[9]

In this present study, the reduction in burning sensation and improvement in inter incisal distance, tongue protrusion and cheek flexibility between the groups was statistically significant at the end of the study. The improvement noted in all the parameters was quite high in the present study compared to the other studies in the management of OSMF. Group II showed improvement in all the parameters progressively. The reason could be that topical Steroids are well recognized to act as immunosuppressive agents causing inhibition of inflammation found in OSMF lesions, thus reducing this fibro-collagenous condition. In addition, steroids can slow down the proliferation of fibroblasts and thus reducing the number of collagen fibers. In early stages of OSMF, curcumin gel provides rapid relief of the symptoms, which was observed in this study.

The dropout rate was equal in both the groups at 30 days, during follow up the number of patients in group 1 was 26 and group 2 was also 26. The symptomatic relief at 30 days for OSMF in Group I and Group II was rapid, which could be the reason for loss to follow up in the study. Lack of awareness, sociocultural influence, and issues of accessibility can be identifified as the main reasons for failures of cessation programs.Various reasons including cultural beliefs, social misconceptions, lack of policies, and lack of research, many people are unaware of the possible harmful efffects of areca nut.^[48]

Limitations of the study

- 1. A potential limitation of the study is that loss to follow up in the study participants
- 2. The outbreak of covid-19 pandemic and the government declared lock down.
- 3. Constant awareness from the government and hospital authorities regarding the spread of covid through saliva caused fear among patients.
- 4. Patients were covid positive hence they dropped out from the study.

5. Awareness and knowledge towards the ill effects of chewing pan, tobbacco, areca nuts usage was less and also due to lower socio economic status. Areca nut is considered as a divine fruit and its usage has an important place in social and cultural customs. Areca nut has addictive potential and an individual who starts this habit in early age becomes addicted in their adulthood.

Future recommendations

Long-term studies with large sample size in the form of randomized controlled trails are recommended in the future to determine the effect and potential of Curenext gel in the management of **OSMF**. Also to understand the efficacy better along with its various mechanism of actions further studies are required.

CONCLUSION

Oral sub-mucous fibrosis is a chronic and a well recognized potentially malignant disorder associated with areca nut chewing, and is prevalent in south Asian population. Pathogenesis of OSMF is not yet established but is believed to be due to multifactorial causes, hence the treatment of oral sub mucous fibrosis postulates a major challenge for an oral medicine specialist. Treatment of OSMF has largely been symptomatic and is associated with high recurrence rate. Curcumin has antiinflammatory, antioxidant, antifibrotic and antitumor activities. All such properties of Curcumin suggest the possibility of its use in the management of oral submucous fibrosis. The clinical response to curcumin gel was comparable to triamcinolone acetonide 0.5% gel. Easy availability, low cost, safer to use with no serious side effects and non invasiveness attributes of curcumin make it an alternative, effective choice of treatment in the management of OSMF.

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TO WHOMSOEVER IT MAY CONCERN

Since Abbott has no role in this study, the investigator is allowed to purchase our product from market & use/study it.

 Dr. Yogesh Sharma
 Abbott Healthcare Pvt. LtdO: 000

 Medical Advisor
 Floor 18, Godrej BKC, Multitherapy & Allevia divisidio t No. C - 68, BKC, Near MCA Club, Bandra (B):ww.abbott.com Mumbai - 400 051
 M: 9987373224

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