



EFFICACY OF CURCUMIN AS LOZENGES IN ORAL SUBMUCOUS FIBROSIS : A PROSPECTIVE STUDY.

Dental Science

Dr. Nimmi Singh*	Department Of Dentistry, IGIMS, Sheikhpura, Bailey Road, Patna 800014 *Corresponding Author
Dr. Devika Singh	Department Of Dentistry, IGIMS, Sheikhpura, Bailey Road, Patna 800014
Dr. Navin Mishra	Department Of Dentistry, IGIMS, Sheikhpura, Bailey Road, Patna 800014
Dr. Arbind Sharma	Department Of Dentistry, IGIMS, Sheikhpura, Bailey Road, Patna 800014

ABSTRACT

Aim & Objectives: The Aim was to clinically study the efficacy of curcumin lozenges in OSMF patients. The objectives were to clinically compare the reduction in burning sensation and improvement in interincisal distance (IID) in study groups under treatment with time.

Material & Methods: The study was carried out for a period of 3 months during which a total of 60 subjects were clinically diagnosed with OSMF Grade I and Grade II, interincisal distance of less than 35mm (according Lai.D.R. classification) & in the age range of 20-45 years. This study was observational and analytical in nature. The detail clinical evaluation was done and stage of OSMF were determined. Demographic data was noted.

Result: 60 participants were included in the study. Visual Analogue Scale (VAS) for burning sensation in Grade I, in comparison with Grade II was more but reduced to almost zero, proving patient to be asymptomatic after treatment. Our study showed that there was increase in the interincisal opening (IID) in both Grade I and Grade II after 3 month of curcumin treatment.

Conclusion: It can be concluded that OSMF is associated with ill habits. It is evident from that the combination of cessation of causative habits with Curcumin as lozenges is an effective management in the treatment of OSMF.

KEYWORDS

Curcumin; Lozenges; Oral Submucous Fibrosis; Visual Analogue Scale (VAS); interincisal opening (IID).

Introduction:-

The term Oral Submucous Fibrosis (OSMF) derived from words, oral (meaning mouth), submucousal (meaning below the mucosa of the mouth) and fibrosis (meaning hardening and scarring).¹

OSMF is a chronic debilitating disease of oro-pharyngeal region which is a well recognized predominantly malignant condition of oral cavity. It is associated with arecanut chewing, Panmasal, gutkha chewing and other similar products. Commonly OSMF is characterized by increased production and decreased degradation of collagen fiber in the buccal mucosa, retromolar area and other parts of the oral cavity and pharynx, which causes progressive inability to open the mouth, trismus, resulting in difficulty in eating and hence causing nutritional deficiencies.^{1,2,3} The greatest risk is that it is a potentially malignant disease and there is a positive correlation between it and the development of leukoplakia and carcinoma of the oral cavity.²

OSMF has a multifactorial etiology. Several factors such as chilli consumption, nutritional deficiency state, arecanut chewing, genetic susceptibility, autoimmunity and collagen disorder have been suggested to be involved in the pathogenesis of the condition.¹

Ulcerations, blanching with burning sensation in oral cavity and difficulty in opening mouth are the initial manifestations of OSMF. According to Pindborg it is clinically divided into three stages. In stage I there is stomatitis, erythematous mucosa, vesicles, mucosal ulcer, melanotic mucosal pigmentation and mucosal petechiae. In stage 2, fibrosis occurs in ruptured vesicles and ulcers when they heal. Vertical and circular palpable fibrotic bands are seen in buccal mucosa. Specific findings include trismus, stiff and small tongue, blanched and leathery floor of mouth, fibrotic and depigmented gingiva, rubbery soft palate with decreased mobility, blanched and atrophic tonsils, shrunken band like uvula and sinking of cheek not commensurate with age or nutritional status. In stage 3 there are sequelae in the form of leukoplakia in about 25 percent of cases, speech and hearing deficits because of involvement of tongue, palate and Eustachian tubes.⁴

The various treatment modalities have been tried by non-surgical and surgical approach. The non-surgical treatment modalities use antioxidants (lycopene), iron supplements, curcumin, steroids, placental extract, fibrinolytic agents. However, no definitive and widely accepted treatment is currently available for this condition.³

The most effective medical treatment has been the use of intralesional steroids in its various forms.^{1,5} The most early sign includes formation

of vesicles, accompanied by a juxtaepithelial inflammatory reaction after which hyalinization of the lamina propria⁶. The fibrosis of the muscle causes stiffness of the oral mucosa with increasing difficulty in mouth opening and tongue protrusion resulting in impairment of functions like eating, swallowing, and phonation.^{7,8}

The main aim of the treatment of OSMF is to improve mouth opening and reduce burning sensation. The present study aims to evaluate the efficacy of curcumin lozenges in treatment of Grade I, and Grade II OSMF.

Aim & Objectives the Study :-

Aim : To clinically study the efficacy of curcumin lozenges in OSMF patients.

Objectives:

1. To clinically compare the reduction in burning sensation in study groups under treatment with time.
2. To study the improvement in mouth opening amongst the study groups under treatment with time.

Inclusion criteria:

1. Patients with positive history of chewing of areca nut or one of its commercial preparations.
2. Burning sensation on eating spicy food.
3. Restricted mouth opening equal to or less than 35mm (according to Lai. D.R classification)

Exclusion Criteria:

1. Patients undergoing any surgery or any drug therapy
2. Patients with reduced mouth opening due to any other reasons like TMJ problems, Pericoronitis of lower third molars.
3. Coexisting lesions
4. Patients previously treated for the OSMF.
5. Allergic conditions
6. Patients with chronic illness, diabetes, hypertension, pregnancy, and any kind of allergy.

Material & Method:-

Source of Data :

The present study is designed to be conducted on patients reporting to the outpatient Department of Dentistry at Indira Gandhi Institute of Medical Sciences and Hospital, Patna, Bihar.

Method of collection of data:**Sample Size:-**

The study group comprised of 60 cases each of clinically diagnosed OSMF Grade I and Grade II with interincisal distance of less than 35mm (Lai.D.R. classification) & in the age range of 20-45 years. After the institutional ethical committee clearance, Declaration of Helsinki and a written consent, a detailed history of all the patients was recorded. Potential recruits to our research study had given sufficient information to allow subjects to decide whether or not they want to take part. Patient Information Sheet was signed individually by all subjects.

Procedure:-

The patients were randomly selected from out patient department of dentistry. Altogether 60 subjects were enrolled in the study group (fig1,2). These patients were asked to discontinue all the habits of tobacco or areca usage. Patient received oral curcumin lozenges, three lozenges/day for three months (*curcuma longa 100mg*). Patients received lozenges in the buccal mucosa bilaterally as oral supplement daily upto 3 months. Cases were followed up till 3 months and 6 months. No side effects such as nausea, stomach upsets, diarrhea were reported by any subject. Follow-up Patients were mandated to visit every 15 days till three months of the treatment regimen for Clinical evaluation. During their subsequent visits two parameters were recorded.

1. Objective criteria: Measurement of interincisal distance on maximum mouth opening (IID)
2. Subjective criteria: Visual Analogue Scale (VAS) for burning sensation

Measurement of the mouth opening was done with the help of fibrometer (fig3) and burning mouth sensation was assessed with the help of visual analog scale (VAS), having score ranging from 1 to 10 at every visit. All the above criteria's were evaluated for baseline (objective and subjective criteria before the start of study), till 3 months. Then the treatment was stopped. But further recall follow-up was done at 6 month interval.

Table 2: Tabular Representation Of Visual Analogue Scale Of OSMF Grade I Subjects.

OSMF_Grade I		N	Range	Minimum	Maximum	Mean	Std. Deviation	Skewness
		Statistic	Statistic	Statistic	Statistic	Statistic	Statistic	Std. Error
VISUAL ANALOGUE SCALE	Vas_0day	26	6.00	4.00	10.00	7.3462	1.49512	-.572
	Vas15days	26	6.00	3.00	9.00	6.2308	1.58260	-.412
	Vas30days	26	5.00	2.00	7.00	4.8077	1.49718	-.342
	Vas60days	26	5.00	1.00	6.00	3.0769	1.49461	.092
	Vas90days	26	5.00	.00	5.00	1.0000	1.32665	1.448

It was observed that the mean baseline Inter Incisal Distance at 0 day was 30.9mm, at 15 days 31.7mm, at 30 days 33.0mm, at 60 days 34.3mm and at 90 days it was 35.7mm. It was observed IID of Grade I subjects increased upto approximately 5mm from baseline to 90 days. Table 3

Table 3: Tabular representation of Inter Incisal Distance (IID) of OSMF Grade I subjects.

OSMF_GRADE I		N	Range	Minimum	Maximum	Mean	Std. Deviation	Skewness
		Statistic	Statistic	Statistic	Statistic	Statistic	Statistic	Std. Error
INTER INCISAL DISTANCE(IID) in mm	IID_ 0 days	26	15.00	20.00	35.00	30.9808	3.52273	-2.033
	IID- 15days	26	16.00	20.00	36.00	31.7308	3.50494	-2.323
	IID_ 30days	26	17.00	21.00	38.00	33.0192	3.68912	-2.135
	IID_ 60days	26	18.00	21.00	39.00	34.3077	3.78174	-2.326
	IID_ 90days	26	19.00	22.00	41.00	35.7692	3.85027	-2.269
	Valid N (listwise)	26						

The mean statistics of Grade II VAS at 0 days was 6.5, VAS at 15 days was 6.0, VAS at 30 days 4.5, at 60 days 3.1 and at 90 days 1.2 respectively. The VAS score comparatively reduced from baseline 0 days to 90 days. It was statistically significant Table 4

Table 4: Tabular representation of visual analogue scale of OSMF Grade II subjects.

OSMF_Grade II		N	Range	Minimum	Maximum	Mean	Std. Deviation	Skewness
		Statistic	Statistic	Statistic	Statistic	Statistic	Statistic	Std. Error
VISUAL ANALOGUE SCALE	Vas_0day	34	6.00	4.00	10.00	6.5000	1.60019	.566
	Vas15days	34	5.00	4.00	9.00	6.0294	1.26695	.322
	Vas30days	34	7.00	2.00	9.00	4.5882	1.45888	.966
	Vas60days	34	6.00	1.00	7.00	3.1176	1.36548	1.293
	Vas90days	34	6.00	.00	6.00	1.2647	1.33278	2.010

It was observed that the mean baseline Inter Incisal Distance at 0 day was 23.0mm, at 15 days 23.5mm, at 30 days 24.6mm, at 60 days 26.0mm and at 90 days it was 27.3mm. It was observed that IID of Grade II subjects increased upto approximately 4mm from baseline to 90 days. Table 5

**Fig.1****Fig.2****Fig.3****Statistical analysis:**

Statistical analysis was done. The results were statistically evaluated by simple frequency table format by EpiInfo software. Descriptive statistics was calculated; mean scores and standard deviation was obtained.

Results

Descriptive Statistics showed that Out of 60 OSMF participants, 26-N of the subjects belonged to Grade I, 34 N belonged to Grade II.

In Gender wise frequency, it was observed that in OSMF Grade I, 84.6% belonged to male category whereas 15.4% belonged to female category. In OSMF Grade II there were 94.1% male and 5.9% female. Statistically both the grades of OSMF were more prevalent in Males. Table 1

Frequency Table 1 Gender**TABLE 1: Tabular representation of Gender wise frequency Grade I and Grade II subjects.**

OMF_Grade		Frequency	Percent	Valid Percent	Cumulative Percent
Grade-I	Valid Male	22	84.6	84.6	84.6
	Female	4	15.4	15.4	100.0
	Total	26	100.0	100.0	
Grade-II	Valid Male	32	94.1	94.1	94.1
	Female	2	5.9	5.9	100.0
	Total	34	100.0	100.0	

The mean statistics of Grade I VAS, 0 days was 7.3, VAS at 15 days was 6.2, VAS at 30 days 4.8, at 60 days 3.0 and at 90 days 1.0 respectively. The VAS score comparatively reduced from baseline 0 days to 90 days. It was statistically significant. Table 2

Table 5: Tabular representation of Inter Incisal Distance (IID) of OSMF Grade II subjects.

OSMF_Grade II		N	Range	Minimum	Maximum	Mean	Std. Deviation	Skewness	
		Statistic	Statistic	Statistic	Statistic	Statistic	Statistic	Statistic	Std. Error
INTER INCISAL DISTANCE(IID) in mm	IID_0 days	34	9.00	20.00	29.00	23.0294	2.98973	.599	.403
	IID_15days	34	10.00	20.00	30.00	23.5735	3.01042	.407	.403
	IID_30days	34	10.00	21.00	31.00	24.6471	3.18978	.372	.403
	IID_60days	34	12.00	21.00	33.00	26.0735	3.51217	.295	.403
	IID_90days	34	14.00	22.00	36.00	27.3235	3.59056	.308	.403
	Valid N (listwise)	34							

In Descriptive Statistics of Age and Duration Of Habit, it was observed that in Grade I the mean age was 33.5 and mean duration of habit in years was 3.2yrs. Whereas in Grade II the result showed mean age 32.1 and duration of habit 4.3yrs. This showed that in Grade II in comparison to Grade I duration of habit was statistically more. Table 6

Descriptive Statistics Age And Duration Of Habit

Table 6: Tabular representation of Age wise and Duration in years of habit among Grade I and Grade II subjects p-value was also highly significant

OSMF		N	Range	Minimum	Maximum	Mean	Std. Deviation	Skewness	
		Statistic	Statistic	Statistic	Statistic	Statistic	Statistic	Statistic	Std. Error
Grade-I	AGE	26	25	20	45	33.54	8.396	-.347	.456
	DURATION IN YEARS	26	8.00	1.00	9.00	3.2115	2.29422	1.066	.456
	Valid N (listwise)	26							
Grade-II	AGE	34	25	20	45	32.18	7.030	.137	.403
	DURATION IN YEARS	34	7.00	1.00	8.00	4.3559	1.82909	.322	.403
	Valid N (listwise)	34							

Wilcoxon Signed ranks test was performed for VAS and IID which proved the P value .000, which was statistically significant. Table 7

Test Statistics^c

Table 7: Tabular representation of VAS and IID among Grade I and Grade II subjects showing p-value .000 which is statistically significant.

	VAS 90 days- VAS 0 day	IID mm 90 days - IIDmm 0 day	P- value
Z	-6.764 ^a	-6.767 ^b	Statistically
Asymp. Sig. (2-tailed)	.000	.000	Significant.

a. Based on positive ranks

b. Based on negative ranks

c. Wilcoxon Signed ranks test

DISCUSSION

Oral submucous fibrosis (OSMF) was first mentioned in the early 1950s. It is said to be a potentially malignant condition which is characterized by stiffness of mucosa and restricted mouth opening caused by changes in fibers of the connective tissue and deeper parts. This pre malignant condition is more prevalent in people of Asian descent.⁶ The literature reveals that patients suffering from OSMF are at an increased risk of developing oral cancer. The malignant transformation rate of OSMF has been reported to be around 7.6%^{3,13}.

In the present study, Curcumin Lozenges 100mg was given three times a day to the patient daily for 90 days. This treatment modality showed significant improvement in reducing the burning sensation in patients which was measured on VAS scale and measurement of interincisal distance on maximum mouth opening (IID) was taken by fibrometer. Our results were found to be in consistent with various other studies quoted in the literature.

In our study, a total of 60 OSMF patients were included out of which, 26-N of the subjects belonged to Grade I, 34 N belonged to Grade II. In Gender wise frequency, it was observed that in OSMF Grade I 84.6% belonged to male category whereas 15.4% belonged to female category. This could be due to the fact that males consume more tobacco in India and also because females probably might not have the liberty to go out for a medical checkup and for the fear, that being a female she might be judged by the society. In OSMF Grade II there were 94.1% male and 5.9% female;. Statistically both Grade I and Grade II of OSMF were more prevalent in Males.

In our present study It was observed that IID of Grade I subjects increased upto approximately 5mm and Grade II subjects increased upto 4mm approximately. Our study showed that there was increase in the interincisal opening after 3month of curcumin treatment. This study was concurrence with S. Kapoor et al (2019) which stated that after administration of curcumin for 3 months, there was a significant

increase in mouth opening⁹. This could be due to the fact that only Grade I and Grade II patients were included where the IID is not much compromised and degree of fibrosis is not as severe as Grade III and Grade IV.

In our present study It was observed that comparatively in Grade I The mean VAS score reduced from 7.3 to 3.0 and in Grade II 6.5, mean VAS 6.0 to 1.2 respectively from baseline 0days to 90 days. This study showed that the Subjective criteria, Visual Analogue Scale (VAS) for burning sensation in Grade I, in comparison with Grade II was more but reduced to almost zero, proving patient to be asymptomatic after treatment. Statistically significant improvement was observed. Our study was coherent to M Yadav et.al(2014) who conducted a study with curcumin and stated that complete resolution of burning sensation was noted.¹⁰. Our study is concordance with Mamta Sharma et al (2017) which stated that there is decrease in burning sensation on VAS scale after treatment¹¹. The significant drop in burning sensation could be attributed to the fact that in Grade I and Grade II, the degree of fibrosis is much less and the blood vessels are not as constricted as Grade III and Grade IV. The other possible explanation could be that in Grade I and Grade II the number of vesicles are more which take lesser time to heal whereas in the other two grades, the erosions due to trauma from tobacco chewing are more, as the flexibility of cheek is reduced and blood supply is compromised resulting in increased chances of trauma and reduced rate of healing.

In Our study it was observed that age and duration of habit, in Grade I the mean age was 33.5 and mean duration of habit in years was 3.2yrs. Whereas in Grade II the mean age 32.1 and duration of habit 4.3yrs. It is proved that even at younger age if the duration of habit is prolonged the chances of transformation into higher grades will be more.

Thus, the management of OSMF poses a great challenge.¹² One new treatment modality which is gaining recognition is the use of turmeric in OSMF. Curcumin (curcuma longa) is a medicinal plant¹³. A number of studies are being conducted all over the world to seek the potential of turmeric and its active component, curcumin, as a chemopreventive agent^{14,15,16}. Our study proved that curcumin lozenge 100mg used thrice for three month showed excellent result. There was complete resolution of burning sensation and a significant increase in mouth opening in both Grade I and Grade II OSMF patients.

CONCLUSION

It can be concluded that OSMF is associated with various forms of tobacco associated habits. Curcumin provide rapid symptomatic relief. It possesses excellent anti-inflammatory and anti-fibrotic properties and anti oxidant properties. However it is non invasive, with minimal side effects, cost effective treatment. It is evident from that the combination of cessation of causative habits with Curcumin is an effective management in the treatment of OSMF in future. Our study proves the efficacy of the curcumin as a potent remedy in OSMF, Further longer term, larger scale studies with higher doses are

recommended to confirm the findings of this report.

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