



EFFICACY OF CURCUMIN IN THE TREATMENT OF OSMF- A CASE-CONTROL STUDY

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ABSTRACT

OSMF is a major health problem affecting more than 2.5 million Indian populations under the age of 40 years and is the most poorly understood and unsatisfactorily treated disease. With the alarming rise in the incidence of OSMF there is an urgent requirement for an effective and safe remedy because of limitations of present therapies to either provide a complete cure or treating the patients at the cost of adverse effects. Curcumin due to its anti-inflammatory, antioxidant and anti-carcinogenic properties can be used in patients with OSMF as application of it is beneficial and inexpensive too.

Method: 20 clinically diagnosed OSMF patients were included each in the study and control group. The study group was prescribed to apply topically commercially available curcumin gel thrice daily. The 20 participants in the control group were not administered any treatment apart from counseling to quit the habit. All the participants were evaluated on the basis of VAS of burning sensation, mouth opening, blanching and fibrous bands on palpation in the recall visits

Results: There was statistically marked reduction in VAS of burning sensation and blanching. Noticeable mouth-opening and reduction in fibrous bands were also observed.

Conclusion: The choice of curcumin therapy is beneficial, affordable and noninvasive to those affected with OSMF. The observations of the present study are very encouraging and appear to be very effective in the treatment of oral submucous fibrosis.

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INTRODUCTION

Oral submucous fibrosis, first described in the early 1950s, is a potentially malignant disease predominantly seen in people of Asian descent.¹ Joshi named the condition as submucous fibrosis (OSMF) in 1953.² In 1956, Paymaster was the first one to describe the precancerous nature of OSMF when he noticed a slow-growing squamous cell carcinoma (SCC) in one-third of the patients diagnosed with the disease.³

With the alarming rise in the incidence of OSMF there is an urgent requirement for an effective and safe remedy because of limitations of present therapies to either provide a complete cure or treating the patients at the cost of adverse effects.

In India where more than 75% of the population cannot afford modern medicine, it would be good time to foray into the medicinal use of the ancient medicine.² Plants have been a major source of medicine since the time immemorial. Turmeric, has been attributed a number of medicinal properties in the traditional systems of medicine. Turmeric and its active ingredient, "curcumin" are being studied upon as chemopreventive agents in India and abroad.⁴

Curcumin (diferuloylmethane) is a polyphenol compound isolated from ground rhizomes of the plant (*Curcuma longa*) L. (Zingiberaceae) found in South Asia. Curcumin exhibits a big promise as a therapeutic agent due to its properties.

Curcumin has been used extensively in ayurvedic medicine for centuries, as it is nontoxic and has a variety of therapeutic properties including antioxidant, analgesic, anti-inflammatory, antiseptic activity, anticarcinogenic activity, chemopreventive, chemotherapeutic activity, anti-tumour, antiviral, antibacterial, antifungal properties and antiplatelet activity.⁵

Sample and method

The present study was conducted in the Department of Oral Medicine and Radiology, Darshan Dental College and Hospital, Udaipur. Individuals with a clinical diagnosis of Oral Submucous Fibrosis according to WHO were included in the study, after obtaining an informed consent and approval of Hospital Ethical Committee. Criteria for selection included a positive history of chewing areca nut or one of its commercial preparations.

Exclusion criteria

1. Individuals who had taken any form of treatment earlier for clinically diagnosed OSMF.
2. Individuals with chronic illness, pregnancy and allergy especially to curcumin.

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3. Individuals diagnosed with scleroderma or with a history of radiotherapy for oral cancer.
4. Individuals who refused to quit habit.

The case control study included 40 participants diagnosed with OSMF, out of which 20 were in study group and 20 in the control group. The control group included participants who were ready to quit the habit and recalled for comparative assessment. No treatment was given.

A custom made case history performa was made which included the details of habit and oral examination. The participants were evaluated on the basis of intensity of burning sensation, inter-incisal mouth opening, blanching and the presence and thickness of palpable fibrous bands.

The intensity of burning sensation was determined using a numerical rating scale of Visual Analogue Scale (VAS) of 0-10 with 10mm division, where 0 indicated no burning sensation and 10 indicated the worst possible burning sensation.

The inter-incisal mouth opening was measured using a divider and a scale from the mesio-incisal angle of upper central incisor to the mesio-incisal angle of lower central incisor and recorded in millimeters. A normal mouth opening of 40-55mm (Bricker *et al*) was considered normal.

Blanching was assessed visually. Fibrous bands were palpated by palpatory method and assessed as presence and thickness of the bands.

All the participants of the study and control group were educated and counseled to quit habit completely. The 20 participants in the study group were given commercially available curcumin gel containing 10mg of curcuma longa extract as the main ingredient with added colours. Therapeutic iron supplements were prescribed for participants whose haemoglobin was less than normal (13.5-17.5gm% in males and 11-15gm% in females).

The participants were asked to take about 1cm length of curcumin gel on their fore finger and massage it gently on the buccal mucosa bilaterally and upper and lower labial mucosa. The patients were instructed to refrain from eating or drinking and swallowing or spitting saliva for 15-20mins post application of the curcumin gel. The outcome was tabulated and statistical analysis was done using Kramer-Tukey test and unpaired t-test.

RESULT

Variables

The variables (age, number of packets per day, frequency of consumption in a day, duration of chewing of one packet, duration of the habit and haemoglobin) was statistically analyzed between the control and the study group. The difference was not considered statistically significant except the number of packets consumed per day in control and study group.

Parameters

The participants were assessed at first, second and third visits for the following parameters- burning sensation, mouth opening, blanching and fibrous bands. The visits were designated as V0 (initial visit), V1 (first recall visit), V2

(second recall visit) and V3 (third recall visit) and henceforth will be mentioned as designated.

Burning sensation

There was no reduction in the intensity of burning sensation in the control group at the end of V3. There was statistically significant reduction in the intensity of burning sensation between V0 and V3 in the study group (Table 1). On comparing the V3 of the control and study group using unpaired t-test, the two tailed p-value was <0.0001, which is considered extremely significant statistically.

Table 1 Comparison of burning sensation

Comparison	p-value	
	Control group	Study group
V0 vs. v3	p>0.05 (non-significant)	P<0.001 (significant)

Mouth opening

The average mouth opening in the control group in V0 was 27.25mm and in V3 was 27.62mm. The average mouth opening in the study group in V0 was 24.9mm and in V3 was 29mm. On comparing the mean differences in the mouth opening between V1, V2, V3 with V0 of the control and study group, there was no significant change (p>0.05). Though there was progressive improvement in mouth opening in the study group, it was not statistically significant.

Blanching

It was observed during the study that the blanching of mucosae improved in a specific pattern in the study group. For convenience, the blanching of the oral mucosa was graded as

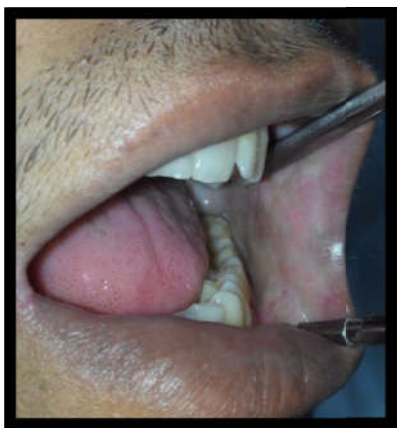
- 0- Normal healthy mucosa
- 1- Diffused areas of healthy mucosa
- 2- Patchy areas of healthy mucosa
- 3- Pinpoint areas of healthy mucosa
- 4- Completely blanched mucosa.



0-Normal Healthy Mucosa



1-Diffused Areas of Healthy Mucosa (more than 1cm)



2-Patchy Areas of Healthy Mucosa (less than 1cm)



3-Pinpoint Areas of Healthy Mucosa



4-Completely Blanched Mucosa

There was no improvement in the blanching of oral mucosae (buccal mucosa, labial mucosa, hard palate, soft palate, faucial pillars, floor of the mouth and ventral surface of the tongue) in the control group. As there was no difference in the mean between V0 and V3, statistical analysis was not possible. There was significant reduction in the blanching of oral mucosae in the study group (Table 2).

Table 2 Comparison of blanching in the study group

Surface	Comparison	p-value
Oral mucosa*	V0 vs. V3	P<0.001 (significant)

*Oral mucosa was separately assessed as under buccal mucosa, labial mucosa, hard palate, soft palate, faucial pillars, floor of the mouth and ventral surface of the tongue. The statistical result arrived at for the different sites were the same in the study group.

On comparing the cumulative mean of improvement in blanching of all the oral mucosal surfaces of the study and

control group using unpaired t-test, the two tailed p-value was 0.03 and by conventional criteria, the difference is considered statistically significant.

Fibrous bands

In the control group, there was no reduction in the thickness of fibrous bands.

Study group

Table 3 Comparison of fibrous bands in the study group

Bands	V0	V3		
		Reduction	Disappearance	Lost to follow-up
Multiple thin bands in right buccal mucosa	8 out of 20 participants	6 out of 8 participants	2 out of 8 participants	-
Multiple thin bands in left buccal mucosa	7 out of 20 participants	5 out of 7 participants	1 out of 7 participants	1 out of 7 participants
Thick bands in right buccal mucosa	10 out of 20 participants	6 out of 10 participants	1 out of 10 participants	3 out of 10 participants
Thick bands in left buccal mucosa	13 out of 20 participants	8 out of 13 participants	1 out of 13 participants	4 out of 13 participants
Circumoral bands	9 out of 20 participants	-	7 out of 9 participants	2 out of 9 participants
Linear horizontal bands	1 out of 20 participants	-	1 out of 1 participant	-

Multiple thin bands

40% of total participants presented with multiple thin bands in the right buccal mucosa in V0. In V3, 75% showed reduction in thickness and 25% showed complete disappearance of thin bands in right buccal mucosa.

35% of total participants presented with multiple thin bands in the left buccal mucosa in V0. In V3, 71.4% showed reduction in thickness and 14.28% showed complete disappearance of thin bands in right buccal mucosa. Rest did not return for evaluation in V3.

Thick bands

50% of total participants presented with thick bands in the right buccal mucosa in V0. In V3, 60% showed reduction in thickness and 10% showed complete disappearance of thick bands in right buccal mucosa. Rest did not return for evaluation in V3. 65% of total participants presented with thick bands in the left buccal mucosa in V0. In V3, 61.53% showed reduction in thickness and 7.7% showed complete disappearance of thick bands in left buccal mucosa. Rest did not return for evaluation in V3.

Circumoral bands

45% of total participants presented with circumoral bands in V0. In V3, 77.77% showed complete disappearance of circumoral bands. Rest did not return for evaluation in V3.

Linear horizontal bands

In the present study linear horizontal bands in the lower buccal vestibule were also found. In the study group, 5% of total participants presented with linear horizontal bands in V0. In

V3, 100% showed complete disappearance of linear horizontal bands.

DISCUSSION

Curcumin has been used extensively in ayurvedic medicine for centuries. It is nontoxic and has a variety of therapeutic properties including antioxidant, analgesic, antihyperalgesic, anti-inflammatory, antiseptic activity, anticarcinogenic activity, chemopreventive, chemotherapeutic activity, anti-tumour, antiviral, antibacterial, antifungal properties and antiplatelet activity.⁵

The vanilloid moiety of curcumin is important for activation of the transient receptor potential vanilloid 1 (TRPV1), which plays an important role in nociception. Curcumin blocks TRPV1 activation in a competitive manner and thereby inhibits TRPV1-mediated pain hypersensitivity.⁶

Turmeric has been described as a dual inhibitor of arachidonic acid metabolism, as it inhibits both cyclooxygenase and lipoxygenase pathways of inflammation, thus inhibiting the products of inflammation such as prostaglandins, leukotrienes. It reduces inflammation by lowering histamine levels and by possibly increasing the production of natural cortisone by adrenal glands.

The mechanism of action by which curcumin shows inflammatory effect is by attenuating inflammatory response of TNF- α stimulated human endothelial cells by interfering with NF- κ B.

Furthermore, curcumin is also capable of preventing platelet derived growth factor (PDGF). Several studies have shown that curcumin has a strong capability for scavenging superoxide radicals, hydrogen peroxide and nitric oxide (NO) from activated macrophages, reducing iron complex and inhibiting lipid peroxidation. It has been shown to scavenge various reactive oxygen species produced by macrophages (including superoxide anions, hydrogen peroxide and nitrite radicals) both *in vitro* as well as *in vivo*. These actions may be the major mechanism by which curcumin exhibits its antioxidant activities.

It has been reported in a study that Curcumin inhibits cell proliferation in fibroblasts and myofibroblasts. MTT assay revealed that curcumin treatment significantly decreases the proliferation of fibroblasts and myofibroblasts, in a dose-dependent manner. This effect is more pronounced in myofibroblasts; the growth inhibitory rate for myofibroblasts incubated curcumin was double of that for the similarly treated fibroblasts. Curcumin induces cell cycle arrest in myofibroblasts. Cell cycle analysis shows that curcumin treatment results in a dose-dependent increase in the proportion of myofibroblast cells in G0/G1 phase. Curcumin induces cell apoptosis in myofibroblasts.⁷

In the present study, there was significant reduction in burning sensation and blanching of oral mucosae. Though there was reduction in the thickness of fibrous bands, no statistically significant improvement in mouth opening was noted. A study concluded that the reduction in the burning sensation with normal and spicy food was due to the scavenging effect of curcumin on superoxide radicals, hydroxyl radicals and lipid peroxidation. Another study was conducted to check the efficacy of turmeric in 30 OSMF patients. An improvement in mouth opening and burning sensation was noticed. Studies

conducted to evaluate the efficacy of curcumin and turmeric dispensed in two forms namely curcumin capsules and turmeric oil in 48 patients with OSMF concluded that statistically significant improvement was observed in the clinical signs and symptoms of patients treated with curcumin and turmeric oil. It showed anti-inflammatory action and fibrinolytic properties. Zhang SS *et al.*, showed in their study that curcumin inhibits proliferation, disrupts the cell cycle, induces apoptosis, and decreases the expression levels of type I and III collagen; confirming its potential therapeutic value in OSMF patient.⁵

CONCLUSION

Curcumin has been used as a therapeutic agent since ages. However, there is not enough information and research in the field of potentially malignant disorders especially OSMF, and therefore, further research is required to determine the efficacy of curcumin. Further investigations with scientific proofs and long-term detailed *in vivo* studies with larger sample size need to be carried out so as to evaluate the efficacy of curcumin in treating Oral Submucous Fibrosis. The observations of the present study are very encouraging and appear to be very effective in the treatment of oral submucous fibrosis.

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