



## TURMERIC AS A TREATMENT MODALITY IN ORAL SUBMUCOUS FIBROSIS – A CLINICAL STUDY

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### ABSTRACT

**Background And Objectives:** Oral Submucous Fibrosis, a potentially malignant condition, irreversible and crippling disease of oral mucosa with no established and successful treatment modality. Turmeric possesses anti-inflammatory, antioxidant, and fibrinolytic properties. Its oncoprevention can be speculated to be due to its protection against DNA damage. It has been shown to favorably alter the serum glutathione and super oxide dismutase activity and reduce lipid per oxidation in patients of OSF. It is being envisaged that incorporation of turmeric in the form of capsules and topical application would greatly enhance treatment of OSF. **Methods:** The present study consisted of 20 subjects with clinical features of OSF and later confirmed histopathologically. The subjects included in the study were randomly divided into two groups of 10 patients each. The patients in Group I were administered curcumin capsules, 3 capsules, thrice daily for 90 days. The patients in Group II were administered turmeric oil topically. **Results:** We observed that turmeric in both capsule and topically applied oil forms was remarkably effective in alleviating all clinical symptoms in all the patients in this study. Remarkable improvement in mouth opening was observed with both forms of turmeric therapy in patients who were in early stages and moderate stages of OSF. Improvements in clinical and histological staging were most notable in stage I and stage II of OSF with both forms of therapy. Although there was no improvement in clinical and histological staging in stage III patients, at least no progression to a worse stage was seen, suggesting that turmeric can help in arresting progression of the disease process. **Conclusion:** We conclude that the patients were extremely pleased with this therapy as they experienced complete relief from clinical symptoms and remarkable improvement in mouth opening. This enabled the patients to resume their relatively normal functions of mastication. This seemed to add to their general feeling of wellbeing. Turmeric is beneficial, well tolerated, non-invasive and affordable and hence may be recommended as a treatment modality in early and moderate stages of OSF and as an adjunct to other treatment modalities in severe cases of OSF.

**KEYWORDS :** OSMF, Turmeric oil, Turmeric capsule

### INTRODUCTION

Disease follows its own rules, neither those of kings nor slaves. Disease is essentially an individual problem and affliction is probably a result of genetic makeup and environmental influences. In India and Southeast Asia, the use of smokeless tobacco in various forms is very popular. This habit, which may be in the form of chewing betel quid, areca nut or pan masala has led to the development of oral submucous fibrosis. In 1966, Pindborg defined OSF as "an insidious chronic disease affecting any part of the oral cavity and sometimes pharynx. Although occasionally preceded by and/or associated with juxta epithelial inflammatory reaction followed by fibro elastic changes in the lamina propria, with epithelial atrophy leading to stiffness of the oral mucosa causing trismus and difficulty in eating"<sup>2</sup>. The prevalence rates of OSF in India range from 0 to 1.2 %. The condition carries a high relative risk for malignant conversion (7.6%) even after the control of the habit. The etiology of OSF is multifactorial: Areca nut (Areca catechu) chewing, the use of chillies, nutritional deficiencies, autoimmunity, and genetic susceptibility have been thought to play an etiological role in OSF. Vitamin A, B, C, iron, and Zinc deficiency have been indicated as possible etiological roles.

Genetic polymorphism predisposing to OSF- polymorphisms of genes coding for TNF-alpha has been reported as significant risk factor for OSF. TNF-alpha is known to stimulate fibroblastic proliferation in vitro providing evidence for an

active role for TNF-alpha in pathogenesis of OSF.<sup>4</sup>

Autoimmunity- has been examined, the reason behind this includes, slight female predilection, occurrence in middle age, the presence of circulating immune complexes, and auto antibodies like anti gastric-parietal cell (GPCA), anti-nuclear anti-reticulin (ANA), smooth muscle (SMA) antibodies

A recent study has revealed higher haplotype frequencies in pairs HLA B51/Cw7 and B62/Cw7 in OSF patients<sup>4</sup>

It has been demonstrated that arecoline and arecaidine, two major areca nut alkaloids, promote collagen formation. Stabilization of collagen fiber, rendering it resistant to degradation by mammalian fibroblast collagenase in oral mucosa and the attendant increase of lysyl oxidase activity also contribute to abnormal deposition of collagen fiber in OSF. Arecoline has shown to be cytotoxic to human buccal fibroblasts in a dose dependent manner by reducing glutathione S transferase activity.<sup>4</sup>

Clinical features of OSF include burning sensation for spicy foods, excessive salivation, dryness of the mouth, defective gustatory sensation and progressive restriction of mouth opening and protrusion of tongue. With the progress of the disease fibrosis may extend from the lamina propria through entire submucosa of the muscle layer. Thick inelastic rope like fibrous bands appear vertically in the buccal mucosa, along

the contours of the faucial pillars and around the entire circle of lips thus leading to difficulty in mouth opening and narrowing of the rima oris. This eventually leads to limited access to the oral cavity that may compromise the oral hygiene and even food intake.<sup>2</sup> OSF is histologically characterized by epithelial atrophy and progressive accumulation of collagen fibers in the lamina propria and submucosa of the oral mucosa. Over the past, various treatment modalities have been attempted for treatment of OSF, which has been concentrated upon attempts to improve the mouth opening by medical or surgical means without satisfactory results.

*Curcuma longa* L, which belongs to the Zingiberaceae family, is a perennial herb distributed throughout tropical and subtropical regions of the world. The major constituent, curcumin (Diferuloylmethane) is the most important fraction of *C. longa* L. Natural curcumin, isolated from *curcuma longa*, contains curcumin I (Diferuloylmethane), as well as curcumin II (6%) and curcumin III (0.3%).<sup>6</sup>

Turmeric capsules and turmeric oil have shown anti-inflammatory, antioxidant, and fibrinolytic actions in OSF patients. They may reverse precancerous changes in oral submucous fibrosis. Its oncoprevention can be speculated to be due to its protection against DNA damage. It has been shown to favorably alter the serum glutathione and super oxide dismutase activity and reduce lipid per oxidation in patients of OSF.<sup>2</sup> Hence the present study was undertaken to assess the effects of turmeric capsules and turmeric oil in the treatment of OSF patients.

#### Objectives Of The Study

- To assess the therapeutic effect of turmeric dispensed in two forms namely turmeric capsules and turmeric oil in OSF patients
- To assess the difference in subjective symptoms, signs, and mouth opening, before and after treatment,
- To assess Histopathological changes before and after treatment

#### MATERIALS AND METHODS

20 patients were selected for the study. These patients were gleaned from among the outpatients, attending M R Ambedkar dental college and hospital. A detailed case history with relevant medical history was recorded. Patients with systemic illness were excluded from the study.

Patients were clinically categorized in to early, moderate, and severe stages, before starting the treatment based on criteria proposed in various studies (Zian RB, Ikeda N, Guptha PC, et al, Bailoor D. N & Nagesh.<sup>21</sup>

#### Clinical Staging

Stage I (early OSMF) - Mild blanching, Normal mouth opening, Tongue protrusion normal, Burning sensation only on taking spicy foods.

Stage II (Moderate OSMF) - Moderate to severe blanching, Mouth opening, and tongue protrusion reduced, Burning sensation even in the absence of stimuli, Palpable bands felt, Unilateral or bilateral lymphadenopathy

Stage III (Severe OSMF) - Severe burning sensation, Marked reduction in mouth opening and tongue protrusion, Ulcerative lesions may appear on the cheek, Thick palpable bands, Lymphadenopathy bilaterally evident.

The degree of mouth opening (the distance between upper and lower incisor) was measured using graduated vernier gauge.

Mobility of tongue was assessed according to the ability to protrude:

- i. Beyond the mucocutaneous junction of the lower lip;

- ii. Only up to vermilion border of lower lip;
- iii. Only up to lower incisal edges

Provisionally subjects were diagnosed as clinically suffering from OSF. Subjects were advised for hematological investigations, following which Biopsies were taken from the right buccal mucosa at the level of occlusal plane. The biopsy specimens thus collected were fixed in 10% formalin and embedded in paraffin.<sup>5</sup> micrometer serial sections were taken using rotary microtome. The slides were stained with Hematoxylin and Eosin. Based on histopathologic report of Hematoxylin and Eosin, the biopsies were grouped according to the criteria of Pindborg JJ and Sirsat SM (1966) in to 4 stages, namely<sup>3</sup>

**Very Early Stage:** Finely fibrillar collagen dispersed with marked edema. Fibroblasts, blood cells are dilated and congested, PMNs, eosinophils.

**Early Stage:** Early Juxta epithelial hyalinization, thick separate collagen bundles, moderate fibroblasts, blood vessels dilated and congested, lymphocytes, eosinophils, and occasional plasma cells.

**Moderately Advanced Stage:** Moderately hyalinized collagen, thick collagen bundles separated by residual edema, blood vessels normal or compressed, lymphocytes and plasma cells.

**Advanced Stage:** Completely hyalinized collagen, edema absent, blood vessels completely obliterated or narrowed lymphocytes and plasma cells.<sup>3</sup>

The patients were strictly advised cessation of habits, and oral prophylaxis to remove local irritant. Their willingness to participate in the study was also obtained in the proforma. The patients were also instructed to be on a bland diet. Treatment was started after patients stopped the habit.

The patients included in the study were randomly divided into 2 groups of 10 patients each. The patients in the first group (Group I- 7 males and 3 female subjects) were administered turmeric capsules; they were instructed to take three capsules, thrice daily for 90 days.

The second group of patients (Group II- 5 males and 5 female subjects) were administered turmeric oil, they were instructed to apply the oil topically in the affected sites in oral cavity (photo 2) and hold it in the mouth for 20 minutes, three times daily for 90 days. They were instructed not to eat, drink or gargle for 1 hour after applying the medication.

The patients were asked to report every 10 days for clinical evaluation and to collect the medication.

On subsequent visits, patients were clinically evaluated based on:

1. Subjective reports by the patients on relief from burning sensation, and tolerance to spicy foods was determined.
2. The degree of mouth opening
3. Mobility of tongue
4. Palpable bands of the cheeks: the presence or absence of fibrous bands was determined by palpation of both buccal mucosa
5. Surface texture of the buccal mucosa was determined by palpation using the index finger.

The treatment was carried out for 90 days, during which the clinical observations were recorded. Biopsies were taken after 90 days of treatment from the right buccal mucosa. The slides were stained with Hematoxylin and Eosin. Examination of the prepared specimen was done under light microscope by oral pathologist and the observations were recorded. The

pretreatment and post treatment biopsy were rendered for histopathologic examination.

**Statistical Method Used For The Present Study:**

Paired t-test, and Mann-Whitney test have been used to test the significance.

**Statistical Software**

The statistical software, namely SPSS was used for analysis of the data and Microsoft word and Excel have been used to generate graphs, tables.

**RESULTS**

In the present study of 20 patients (Group I) and (Group II) suffering from OSF, the various parameters are shown as below

Out of 20 cases of OSF studied, 60% cases were males and 40% were females.

**Habit (areca nut chewing) frequency and duration in**

Group I			Group II		
case	frequency	duration	case	frequency	duration
1	8 packets	2 years	1	5 packets	6yrs
2	8 packets	3 years	2	4/day	15yrs
3	3 / day	8 yrs	3	10/ day	2 yrs
4	5/day	7 yrs	4	10/day	5yrs
5	12/day	5yrs	5	10 /day	3yrs
6	-	-	6	13/day	7yrs
7	7/day	3 yrs	7	17/day	9 yrs
8	10/day	4 yrs	8	6/day	3 yrs
9	13/day	5 yrs	9	9/day	4 yrs
10	10/day	2.5 yrs	10	7/day	3 yrs

**SYMPTOMS (burning sensation, intolerance to spicy food and pain on mouth opening)**

Group I			Group II		
case	Pretreatment	Post treatment	case	Pretreatment	Pretreatment
1	Yes	No	1	Yes	No
2	Yes	No	2	Yes	No
3	Yes	No	3	Yes	No
4	Yes	No	4	Yes	No
5	Yes	No	5	Yes	No
6	Yes	No	6	Yes	No
7	Yes	No	7	Yes	No
8	Yes	No	8	Yes	No
9	Yes	No	9	Yes	No
10	Yes	No	10	Yes	No

**Comparison Of Mouth Opening In Pre And Post Treatment Phases In Group I:**

Systemic:

Mouth Opening	Mean	SD	Mean difference	t	P-value
Pre test	1.78	0.86	-0.575	-4.070	0.003
Post test	2.36	1.12			

**Comparison of mouth opening in pre and post treatment phases in group II:**

Topical:

Mouth Opening	Mean	SD	Mean difference	t	P-value
Pre test	2.26	0.67	-0.430	-5.652	<0.001
Post test	2.69	0.82			

**Comparing The Mouth Opening Between Systemic And Topical Group Using T-test.**

Pretreatment:

Mouth Opening	Mean	SD	Mean difference	t	P-value
Systemic	1.78	0.86	-0.480	-1.388	0.182
Topical	2.26	0.67			

Post treatment:

Mouth Opening	Mean	SD	Mean difference	t	P-value
Systemic	2.36	1.12	-0.335	-0.765	0.454
Topical	2.69	0.82			

**Changes in Palpable bands (systemic) group I from pretreatment to post treatment:**

Pretest	N	%	Post Test	N	%
Yes	8	80	Yes	6	60
No	2	20	No	4	40
<b>Total</b>	<b>10</b>	<b>100</b>	<b>Total</b>	<b>10</b>	<b>100</b>

**Changes in Palpable bands in (topical) group II from pretreatment to post treatment:**

Pretest	N	%	Post test	N	%
Yes	6	60	Yes	3	30
No	4	40	No	7	70
<b>Total</b>	<b>10</b>	<b>100</b>	<b>Total</b>	<b>10</b>	<b>100</b>

**Comparison of tongue protrusion in pretreatment and post treatment: Systemic group:**

Tongue Protrusion	Mean	SD	Median	Z	P-value
Pretest	2.10	0.88	2.00	-1.732	0.083
Post test	1.60	0.70	1.50		

**Topical group:**

Tongue Protrusion	Mean	SD	Median	Z	P-value
Pretest	1.50	0.71	1.00	-1.000	0.317
Post test	1.40	0.70	1.00		

**Comparing the tongue protrusion between group I(systemic) and group II (topical) using t-test.**

**Pretest:**

Tongue Protrusion	Mean	SD	Median	Z	P-value
Systemic	2.10	0.88	2.00	-1.582	0.114
Topical	1.50	0.71	1.00		

**Post test:**

Tongue Protrusion	Mean	SD	Median	Z	P-value
Systemic	1.60	0.70	1.50	-1.264	0.206
Topical	1.40	0.70	1.00		

**Comparison of clinical staging in pretreatment and post treatment phases**

**group I:**

Clinical Staging	Mean	SD	Median	Z	P-value
Pretest	1.90	0.57	2.00	-1.732	0.083
Post test	1.60	0.70	1.50		

**group II:**

Clinical Staging	Mean	SD	Median	Z	P-value
Pretest	1.40	0.70	1.00	-1.000	0.317
Post test	1.30	0.67	1.00		

**Comparing the clinical stages between group I and group II using Mann-Whitney test.**

**Pretest:**

Clinical Staging	Mean	SD	Median	Z	P-value
Systemic	1.90	0.57	2.00	-1.880	0.060
Topical	1.40	0.70	1.00		

**Post test:**

Clinical Staging	Mean	SD	Median	Z	P-value
Systemic	1.60	0.70	1.50	-1.211	0.226
Topical	1.30	0.67	1.00		

**Changes in Histopathology from pretreatment to post treatment:**

**Systemic group:**

Pretreatment	N	%
Early	3	30
Advanced	3	30
Moderately Advanced	4	40
<b>Total</b>	<b>10</b>	<b>100</b>
Post treatment	N	%
Very Early	2	20
Early	3	30
Advanced	3	30
Moderately Advanced	2	20
<b>Total</b>	<b>10</b>	<b>100</b>

**Topical group:**

Pretreatment	N	%	Post treatment	N	%
Early	3	30	Very Early	1	10
Advanced	1	10	Early	4	40
Moderately Advanced	6	60	Advanced	1	10
<b>Total</b>	<b>10</b>	<b>100</b>	Moderately Advanced	4	40
			<b>Total</b>	<b>10</b>	<b>100</b>

**DISCUSSION**

The age group of the patients ranged from 21 to 55 years. This finding is in contrast to that of Pindborg et al, who reported the OSF cases in age group of 40-49 years.<sup>1</sup> But our finding is in concurrence with studies conducted by Sirsat and Khanolkar<sup>22</sup> Sinor et al, Shah<sup>11</sup> The present study indicated that most of them suffering from OSF were of younger age group. Traditionally in India, only married adults have been consumers of areca nut. However, during recent years, with the advent of attractive, conveniently packed sachets, mass and media advertisements, consuming of gutkha and pan masala by younger people has increased. The other reason might be easy availability of gutkha and pan masala in every corner as well as a social status evil. Increase in the chewing habit of the areca nut without any tobacco and the use of various commercial products containing areca nut may explain the decrease in the age of the OSF cases due to various chewing habits. The mean age of occurrence was lower in males than in females.

In our study, 17/20 patients were found to be in the lower socioeconomic group. This finding is in conformity with that of Wahi et al<sup>23</sup>, Shiau and Kwan,<sup>24</sup> Ramanathan<sup>25</sup>

In our study group all the patients except one were found to have indulged in the habit of chewing areca nut or commercial areca nut products. Recent epidemiological studies in India point to the habit of chewing areca nut as the major etiological factor of OSF. We found that the patients who used pan masala with greater frequency/ day developed OSF with a shorter duration of habit. This was consistent with observations made by Shah et al, Mehar et al. The findings in the present study, therefore, support the role of areca nut chewing as the single most important factor in the etiology of OSF.

Arecoline present in areca nut induces fibroblastic proliferation and increased collagen formation. The copper content of areca nut up regulates enzyme lysyl oxidase which is responsible for collagen synthesis.

All patients reported the use of rich spices in their diet and one patient reported a high intake of chillies without the habit of chewing areca nut. The possible role of chillies in the etiology of OSF have been suggested by several workers.<sup>11-16</sup> It may be mentioned that chillies can damage the cells of the mucosa and if this is continuous, it probably causes chronic inflammation, which leads to the formation of excessive fibrosis. Chillies have indirect effect on the pathogenesis of OSF as hypersensitivity to chillies is often explained as a common factor in the development of OSF, as observed by Laskaris et al. Because of the excessive use of chillies and spices, as is the case in OSF subjects, along with low nutritional value food, occurrence in lower middle class, it appears that such factors have a cumulative effect on the incidence, nature and severity of the disorder. However, since all patients had the habit of using spices, it is possible that a combination of intake of spices and chewing areca nut have contributed to the causation of OSF. This is in agreement with that of Hamner et al who stated that an allergic reaction or prolonged irritation of oral mucosa by spices and areca nut induced tissue alterations which led to OSF.

On hematological investigation of all patients, hematological parameters were within normal limits for 18 patients. The hemoglobin levels in 2 patients were less, suggestive of anemia. These 2 patients were in the advanced stage of OSF. The reason for the anemia being decreased mouth opening and intolerance to food, which has led to decreased intake of nutritious food and minerals such as iron and zinc etc. This finding has also been observed by Pindborg and Sirsat, Lemmer and Shear, Paissat.<sup>3</sup>

All the patients in the study tolerated the treatment regimens well. None of the patients reported any allergic reactions, nor did we elicit signs or symptoms of toxicity to the treatment modalities. Studies reported by Ricky A Sharma et al, joshi et al, Soni and Kuttan, showed turmeric to be non-toxic.<sup>7,9</sup>

The principal symptom reported by all the patients in Group I (systemic) and Group II (topical) were burning sensation followed by the complaint of intolerance to spicy food and pain on opening mouth. The clinical symptoms were identical to those described by several workers.

In our study, all the 10 patients in Group I (systemic) treated with turmeric capsules and all the 10 patients in Group II (topical) treated with turmeric oil presented a reduction in burning sensation and intolerance to spicy foods, pain on mouth opening and better intake of food within 10 days of initiation of treatment. This shows that turmeric capsules and turmeric oil produced a reasonably early improvement. All Patients in Group I and II were completely free from symptoms such as, burning sensation, intolerance to spicy food and pain on opening mouth after 90 days of treatment, which were the chief complaints of majority of patients. Regression of burning sensation by turmeric capsules and turmeric oil has been reported by Kuttan et al in precancerous lesions<sup>31</sup> and by Hastak et al in Oral submucous fibrosis.<sup>19</sup> The local symptoms of burning sensation and pain were reduced, as observed by Bide SV, Ghasis SD, Hastak.<sup>20</sup>

Geol et al have demonstrated anti-inflammatory properties of curcumin.<sup>18</sup> This was due to suppression of prostaglandin synthesis, and inhibited expression of cox-2. This finding was congruous with reports obtained in the similar studies conducted by Plummer SM, Chen, and RC Lantz.<sup>8</sup>

Pindborg has described, juxta epithelial inflammatory reaction followed by fibroelastic change in lamina propria in his definition of OSF, so inflammation is definitely a component of OSF and anti-inflammatory effects of turmeric capsules and turmeric oil might have brought about the remarkable regression in clinical symptoms after treatment.

Curcumin has been described as a dual inhibitor of arachidonic acid metabolism by inhibiting both cyclooxygenase and lipoxygenase pathways of inflammation, thus inhibiting the products of inflammation such as prostaglandins, leukotrienes as observed by Lantz RC, Ammon, Jobin, Hong.<sup>9</sup>

In the present study, mild to severe restriction in mouth opening was found with varying intensities in all patients in both the groups. This is consistent with findings observed by Rajendran R, Lai DR, Ranganathan K et al.<sup>3</sup>

#### **Comparison of mouth opening in pre and post treatment phases in Group I and Group II:**

In our study, we observed an increase in mouth opening clinically within 15 days of initiation of treatment in Group I and Group II patients. The interincisal mouth opening increased in 8/10 patients in Group I and in 9/10 patients in Group II with varying intensities depending on progression of the disease during and after completion of treatment. There was no change in mouth opening in 2 patients with severe OSF

in Group I and 1 patient with severe OSF in group II. We found that Patients with early stages showed a better improvement than those with severe stages of OSF. This was significant statistically.

The clinical and statistically significant increase in mouth opening brought about by turmeric oil and turmeric capsules can be attributed to anti-inflammatory and fibrinolytic properties as explained earlier in this context. Bhide and Hastak in two different studies also achieved an increase in mouth opening when turmeric capsule and turmeric oil was used in treatment of OSF patients.<sup>19,20</sup>

The most common clinical signs noted in the present study were, blanching of oral mucosa, palpable fibrotic bands in right and left buccal mucosa, and restricted tongue movements with varying intensities as also reported by Whai et al, and Pindborg et al.<sup>1</sup> The limitation of tongue protrusion was observed in majority of patients, similar findings reported by Rajendran R, Khanna JN, and Anrade NN.<sup>14,17</sup>

#### **Changes In Palpable Bands And Tongue Protrusion From Pretreatment To Post Treatment:**

In our study, 2/8 patients who had palpable bands in Group I (treated with turmeric capsules) and 3/6 patients who had palpable bands in Group II (treated with turmeric oil) revealed absence of palpable bands after completion of treatment. This was not statistically significant. 3/10 patients in Group I and 1/10 patients in Group II showed improvement in tongue protrusion after completion of treatment. This was not statistically significant.

Curcumin has been reported to possess fibrinolytic actions in liver and lungs in studies conducted by kuttan et al.<sup>9</sup> nirmala et al<sup>10</sup> showed that curcumin modulates collagen metabolism by free radical scavenging and inhibition of lysosomal enzyme release. Li et al has attributed the fibrinolytic action of curcumin to its, inhibition of lipid peroxidation, checking cellular proliferation, and collagen synthesis. The same action of turmeric may be responsible for reduction in palpable fibrotic bands and improvement in tongue protrusion. The above findings in the study suggest that turmeric may have a fibrinolytic action in OSF.

#### **Comparison Of Clinical Staging In Pretreatment And Post Treatment Phases In Group I And Group II:**

The patients selected in our study were categorized into early, moderate, and severe, clinical stages based on clinical presentation.<sup>21</sup> In Group I there were 2 patients with early features (stage I), 6 with moderate (stage II) and 2 with severe (stage III) OSF. There was improvement in the clinical stage in 5/10 patients in group I.

In Group II there were 7 patients with early features (stage I), 2 with moderate (stage II) and 1 with severe (stage III) OSF. In this only 2/10 patients showed improvement in clinical staging after completion of treatment. This may be explained by the fact that most of the patients in this group were already in stage I (7/10) and there were no criteria prescribed to grade further improvement from stage I. This is one of the limitations of the classification of clinical staging, used in this study.

#### **Comparison Of Histopathological Staging In Pretreatment And Post Treatment Phases In Group I And Group II:**

Histopathological findings of biopsies conducted before initiation of treatment and after 90 days of treatment, were graded and compared. Histopathological features commonly seen in biopsy specimen before treatment included atrophic epithelium, loss of retepegs, intracellular oedema, hyalinization of collagen fibers in connective tissue, obliteration of blood vessels, inflammatory cell infiltrate. The above histological findings are in concurrence with observations made by Pindborg and Sirsat, Utsunomiya H,

Tilakratne WM.<sup>33</sup>

The biopsy specimens were also categorized according to their histologic features in to very early, early, moderately advanced, and advanced OSF. Pretreatment histopathological features revealed that in Group I there were 3 patients with early OSF, 4 with moderately advanced and 3 with advanced OSF. In Group II there were 3 patients with early OSF, 6 with moderately advanced, and 1 with advanced OSF.

Post treatment histopathologic reports of biopsies showed that 4/10 patients in group I and 3/10 patients Group II improved a stage better. There was no change in Histopathologic features in the rest of the patients in both the groups but remained in same stage. This was not statistically significant. The improvement in changes observed were hyperplasia of epithelium, reduction in inflammatory cells, increase in blood vessels, reduced hyalinization.

The histopathologic grading coincided with the clinical scoring in few cases, but in rest of the patients there was no concurrence between clinical scoring and histopathologic scoring. These findings are consistent with findings made by Supriya S Koshti and Suresh Barpande.<sup>21</sup>

Histological changes of hyperplasia of epithelium reduction in inflammatory cells, observed after treatment with turmeric may be considered to be involved in reduction of burning sensation and intolerance to spicy foods. Similarly, reduction in hyalinization of connective tissue and inflammatory cells may be attributed to the improvement in mouth opening and tongue protrusion, in patients treated with turmeric.

Hence, we can conclude from our observations that turmeric in both capsule and topically applied oil forms, was remarkably effective in alleviating all clinical symptoms in all the patients in this study.

Remarkable improvement in mouth opening was observed with both forms of turmeric therapy in patients who were in early stages and moderate stages of OSF.

Improvements in clinical and histological staging were most notable in stage I and stage II of OSF with both forms of therapy. Although there was no improvement in clinical and histological staging in stage III patients, at least no progression to a worse stage was seen, suggesting that turmeric can help in arresting progression of the disease process.

Improvement in clinical staging and histopathological grading was found to be slightly better in response to turmeric capsules than with turmeric oil. This might be due to better systemic absorption of the drug when given orally than on being topically applied. Another drawback of the topical application could be shorter duration of action, owing to it getting washed away by saliva.

Extensive studies involving larger population and longer follow-up evaluation may be required to establish the use of turmeric as a definitive treatment modality in treating OSF.

## CONCLUSION

Oral Submucous Fibrosis, a potentially malignant condition, irreversible and crippling disease of oral mucosa with no established and successful treatment modality, has attained epidemic proportions in the Asian Subcontinent. Various treatment modalities, both surgical and medical, have been unsuccessful in complete amelioration of the clinical signs and symptoms of this disease, leading to ever essential quest for novel ways of therapies for this disease.

The advent of herbal renaissance has produced a profound

effect on the system of medicine. Turmeric, a well-known indigenous herbal medicine is of late being recognized as 'nature's precious gift'. Turmeric, hence, has been introduced as a novel therapeutic modality in treating OSF.

There was significant improvement clinically in the signs and symptoms after treatment in patients of Group I and II with turmeric capsule and oil respectively. There was complete relief from burning sensation, intolerance to spicy foods and pain on mouth opening in all the patients with both forms of therapies. There was a remarkable increase in mouth opening in patients of both groups with mild to moderate stage of the disease. Improvement seen in clinical and histological stages in the patients with mild and moderate forms of the disease is an encouraging finding towards establishing the use of turmeric as a therapeutic agent in such cases. The arrest of progression of the disease process by use of turmeric in both forms may indicate its future use as a potential chemopreventive agent. Thus, the choice of turmeric therapy is beneficial, affordable and a non-invasive treatment modality to those affected with OSF. It is evident from our study that turmeric holds good promise in the treatment of OSF in the future.

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