Efficacy of Turmeric and Tulsi in Management of Oral Submucous Fibrosis

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Abstract

Oral submucous fibrosis is a chronic precancerous condition that affects the oral mucosa leading to stiffness and causes trismus and inability to eat. This is a most common condition seen in young adults abusing oral betel nut and tobacco chewing, mostly prevalent in India and Southeast Asia. Variety of treatment modalities, conservative and surgical, have been tried with no definitive successful outcomes. In recent times, many ayurvedic preparations have been advocated along with conventional conservative treatment modalities. The present study evaluated the efficacy of tulsi and curcumin in management of oral submucous fibrosis when used along with conventional oral antioxidant therapy.

Keywords: *Submucous Fibrosis, Trismus, Tulsi Curcumin*

1. INTRODUCTION

Oral submucous fibrosis (OSMF) is a chronic and high risk precancerous condition. The condition was prevalent in the days of Sushruta (600 BC), a great practitioner of ancient medicine where he labeled this condition as 'Vidhari'. OSMF is an insidious, chronic disease affecting any part of the oral cavity and sometimes pharynx although occasionally preceded by and/or associated with vesicle formation, always associated with juxtaepithelial inflammatory reaction, followed by fibroelastic changes of lamina propria, with epithelial atrophy leading to stiffness of oral mucosa and causing trismus and inability to eat[1]. Epidemiological studies show a unique prevalence of this premalignant condition in India and South East Asia[2]. There are many treatment modalities, medically and surgically, proposed for OSMF but none proved complete cure and reduced morbidity value. Hence the search for an effective treatment modality still continues.

Since the ancient age plants are the major source of medicine. Curcumin is the active ingredient in the traditional herbal remedy and dietary spice turmeric (Curcuma longa). Curcumin has a surprisingly wide range of beneficial properties, including anti-inflammatory and antioxidant. Many of the activities associated with curcumin relate to its ability to suppress acute and chronic inflammation[3] In vitro studies have shown that curcumin inhibits lipo-oxygenase and cyclooxygenase activities in phorbol 12-myristate 13-acetate (PMA)-induced inflammation of mouse fibroblast cells[4], xanthine oxygenase activities in NIH3T3 cells[5]. Tulsi is an aromatic shrub in the basil family Lamiaceae (tribe ocimeae) that is thought to have originated in north central India and now grows native throughout the eastern world tropics[6]. Within Ayurveda, tulsi is known as "The Incomparable One," "Mother Medicine of Nature" and "The Queen of Herbs," and is revered as an "elixir of life" that is without equal for both its medicinal and spiritual properties[7]. Tulsi also helps to prevent cancers caused by toxic compounds by reducing DNA damage[8] and inducing apoptosis in precancerous and cancerous cells, thereby reducing the growth of experimental tumors and enhancing survival[9, 10]. Furthermore, tulsi not only protects against the damage caused by toxic compounds, but also enables the body to more effectively transform and eliminate them by enhancing the activity of liver detoxification enzymes such as the cytochrome P450 enzymes, which deactivates toxic chemicals and enables them to be safely excreted[11].

Due to all these properties, a synergistic approach using both tulsi and curcumin, along with oral antioxidant therapy was planned in the management of OSMF

2. MATERIAL AND METHODS

The prospective observational study was conducted at Bharati Vidyapeeth University Dental College & Hospital, Pune with institutional ethical committee approval. One hundred twenty four patients who were clinically diagnosed with Oral Submucous Fibrosis Grade I and Grade II, irrespective of age, gender, occupation, social status, and ethnicity were included in this study. Patients already undergoing pharmacological or surgical treatment for OSMF were excluded from the study. Patients with systemic diseases were excluded from the study.

All patients were motivated for life style modifications and advised to quit smoking cigarette and bidis, chewing tobacco, gutkha, betel nut, areca nut and alcohol consumption. All patients had some or other habit but most patients had the habit of chewing betel nut, tobacco and gutkha. The herbs (Tulsi and Curcumin) were powdered in pulverizer in ayurvedic pharmacy lab of Bharati Vidyapeeth University Ayurvedic College under the supervision of ayurvedic specialist after conducting pharmacognosy study.

One hundred twenty four patients were divided in two groups (Group A – Study group and Group B – Control group) and each group consisted 62 patients. Group A (Study group) patients were given conventional treatment (Oral antioxidant therapy) along with mixture containing 1 gm of Turmeric powder and 1 gm of Tulsi powder in glycerine for local application and they were instructed to apply the mixture all over the oral mucosa 4-5 times per day and not to eat or drink anything for next 15 minutes. Group B (Control group) patients were given only conventional oral antioxidant therapy. All patients were advised to come for follow-up visits at 1 month interval for 3 months.

Each time burning sensation on Visual Analog Scale (VAS) and Inter-incisal distance was measured (using Vernier calliper) and recorded. Results were statistically analysed at the end of the study by paired 't' test to find out the efficacy of the treatment.

3. STATISTICAL DATA ANALYSIS

The data on categorical variables is shown as n (%) and data on continuous variables is presented as Mean and Standard deviation (SD) across two study groups. The inter-group statistical comparison of means of continuous variables is done using independent sample t test.

Table 1. Inter-group and intra-group comparison of mean mouth opening score

	Group A (Study Group) (n=62)		Group B (Control Group) (n=62)		P-value (Inter-Group)
Mouth opening score (mm)	**Mean ± SD**	**Min – Max**	**Mean ± SD**	**Min – Max**	**Group A vs Group B**
Pre-treatment	28.80 ± 3.12	26 – 36	30.00 ± 2.45	26 – 33	0.351^{NS}
Post-treatment	33.30 ± 3.16	30 – 40	34.00 ± 2.62	30 – 37	0.597^{NS}
% Change At Post-treatment	15.79%	11.1 – 20.7	13.38%	10.3 – 15.6	0.063^{NS}
P-value (Intra-group)					
Pre v Post	0.001^{***}		0.001^{***}		
P-value (Inter-Group) by independent sample t test. P-value (Intra-Group) by paired t test. P-value<0.05 is considered to be statistically significant. ***P-value<0.001, NS-Statistically non-significant.					

The intra-group statistical comparisons are done using paired t test each study group. The underlying normality assumption was tested before subjecting each variable to t tests. All results are shown in tabular as well as Fig.ical format to visualize the statistically significant difference more clearly. In the entire study, the p-values less than 0.05 are considered to be statistically significant. All the hypotheses were formulated using two tailed alternatives against each null hypothesis (hypothesis of no difference). The entire data is statistically analyzed using Statistical Package for Social Sciences (SPSS version 21.0, IBM Corporation, USA) for MS Windows.

Inter-Group Comparisons

The mean ± SD of pre-treatment mouth opening score in Group A (Study Group) and Group B (Control Group) was 28.80 ± 3.12 mm and 30.00 ± 2.45 mm respectively. The distribution of mean pre-treatment mouth opening score did not differ significantly between two study groups (P-value>0.05). (Table 1, Figure 1a). The mean ± SD of post-treatment mouth opening score in Group A (Study Group) and Group B (Control Group) was 33.30 ± 3.16 mm and 34.00 ± 2.62 mm respectively. The distribution of mean post-treatment mouth opening score did not differ significantly between two study groups (P-value>0.05). The mean % change in mouth opening score at post-treatment follow-up in Group A (Study Group) and Group B (Control Group) was 15.79% and 13.38% respectively. The distribution of mean % change in mouth opening score at post-treatment follow-up did not differ significantly between two study groups (P-value>0.05).

Intra-Group Comparisons

In Group A (Study Group)

The distribution of mean pre-treatment mouth opening score is significantly higher compared to mean post-treatment mouth opening score (P-value<0.001).

In Group B (Control Group)

The distribution of mean pre-treatment mouth opening score is significantly higher compared to mean post-treatment mouth opening score (P-value<0.001). (Figure 1b)

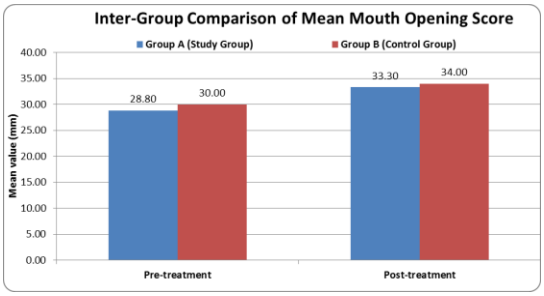

Fig. 1a Inter-group comparison of mean mouth opening score

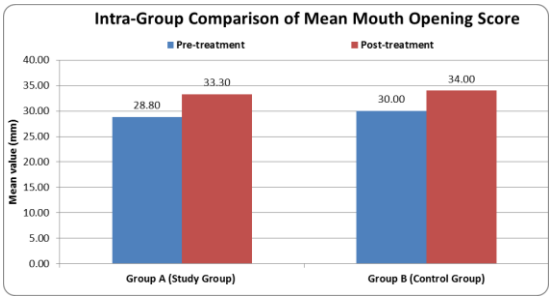

Fig. 1b Intra-group comparison of mean mouth opening score

Inter-Group Comparisons

The mean ± SD of pre-treatment burning sensation score (VAS) in Group A (Study Group) and Group B (Control Group) was 7.30 ± 1.25 and 7.30 ± 0.67 respectively. The distribution of mean pre-treatment burning sensation score (VAS) did not differ significantly between two study groups (P-value>0.05). (Table 2, Fig. 2a)

The mean ± SD of post-treatment burning sensation score (VAS) in Group A (Study Group) and Group B (Control Group) was 3.10 ± 1.29 and 4.00 ± 1.25 respectively. The distribution of mean post-treatment burning sensation score (VAS) did not differ significantly between two study groups (P-value>0.05).

The mean % change in burning sensation score (VAS) at post-treatment follow-up in Group A (Study Group) and Group B (Control Group) was 58.02% and 45.77% respectively. The distribution of mean % change in burning sensation score (VAS) at post-treatment follow-up did not differ significantly between two study groups (P-value>0.05)

Table 2. Inter-group and intra-group comparison of mean burning sensation score (VAS)

	Group A (Study Group) (n=62)		Group B (Control Group) (n=62)		P-value (Inter-Group)
Burning sensation score (VAS)	**Mean ± SD**	**Min – Max**	**Mean ± SD**	**Min – Max**	**Group A vs Group B**
Pre-treatment	7.30 ± 1.25	5 – 9	7.30 ± 0.67	6 – 8	0.999^{NS}
Post-treatment	3.10 ± 1.29	2 – 6	4.00 ± 1.25	2 – 6	0.130^{NS}
% Change At Post-treatment	58.02%	33.3 – 75.0	45.77%	25.0 – 66.7	0.061^{NS}
P-value (Intra-group)					
Pre v Post	0.001***		0.001***		
P-value (Inter-Group) by independent sample t test. P-value (Intra-Group) by paired t test. P-value<0.05 is considered to be statistically significant. ***P-value<0.001, NS-Statistically non-significant.					

Intra-Group Comparisons

In Group A (Study Group)

The distribution of mean pre-treatment burning sensation score (VAS) is significantly higher compared to mean post-treatment burning sensation score (VAS) (P-value<0.001).

In Group B (Control Group)

The distribution of mean pre-treatment burning sensation score (VAS) is significantly higher compared to mean post-treatment burning sensation score (VAS) (P-value<0.001). (Fig. 2b)

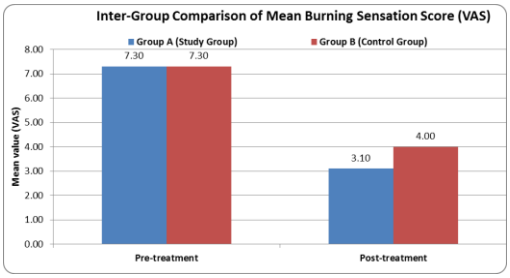

Fig. 2a Inter-group comparison of mean burning sensation score (VAS)

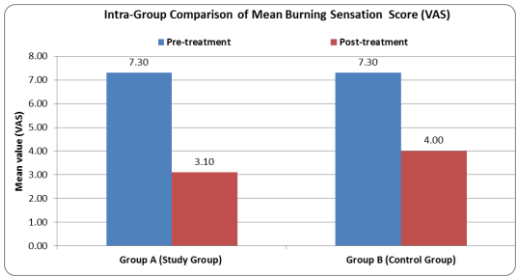

Fig. 2b Intra-group comparison of mean burning sensation score (VAS)

4. DISCUSSION

Oral submucous fibrosis is one of the most poorly understood and unsatisfactorily treated condition. An estimated 2.5 million people suffer from the disease in India and all available treatments give only symptomatic relief which is short lived[12]. Recently, interest in herbal medicines have been increased and various studies are being carried out to explore clinical efficacy of herbal compound preparations. The trial formulations in our study, Tulsi and curcumin, were supplemented with the conventional oral antioxidant therapy to evaluate their synergistic

effect in management of OSMF. Curcumin is known to be strong antioxidant and reduces inflammation. It increases blood circulation and is anti-mutagenic[13, 14].

Curcumin was first isolated by Vogel in 1842 and structurally characterized by Lampe and Milobedeska in 1910[15]. It was synthesized and confirmed in 1913[16]. Typical extracts of Curcuma longa L contain the structures I–III, of which I is the most common[17]. Reports conflict as to whether I or III is the most potent as an antioxidant and anti-tumor agent[14, 17]. Curcumin exists in its enol-tautomer form[18] and it exhibits limited solubility in water, slight solubility in MeOH, and good solubility in DMSO and chloroform, a property that may be responsible for its low bioavailability.

In addition to a role as a chemopreventive and chemotherapeutic agent, curcumin may also function as a chemosensitizer, enhancing the activity of other anti-neoplastic agents, in part by inhibiting pathways that lead to treatment resistance[19].

Curcumin inhibits cancer development and progression, targeting multiple steps in the pathway to malignancy. Curcumin has activity as both a blocking agent, inhibiting the initiation step of cancer by preventing carcinogen activation, and as a suppressing agent, inhibiting malignant cell proliferation during promotion and progression of carcinogenesis[20].

Tulsi is an aromatic shrub in the basil family Lamiaceae (tribe ocimeae) that is thought to have originated in north central India and now grows native throughout the eastern world tropics[21]. Within Ayurveda, tulsi is known as "The Incomparable One," "Mother Medicine of Nature" and "The Queen of Herbs," and is revered as an "elixir of life" that is without equal for both its medicinal and spiritual properties[22].

The anti-inflammatory action of tulsi, which has been observed in both acute and chronic inflammatory models in animals,[23,24,25] is attributed to tulsi's eugenol and linoleic acid content and the inhibition of both the cyclooxygenase and the lipoxygenase pathways of arachidonic acid metabolism[26,27]. This enables tulsi to exert anti-inflammatory effects comparable to nonsteroidal anti-inflammatory drugs such as phenylbutazone, ibuprofen, naproxen, aspirin and indomethacin[28]. Tulsi also helps to prevent cancers caused by toxic compounds by reducing DNA damage[8] and inducing apoptosis in precancerous and cancerous cells, thereby reducing the growth of experimental tumors and enhancing survival[8,9]. Furthermore, tulsi not only protects against the damage caused by toxic compounds, but also enables the body to more effectively transform and eliminate them by enhancing the activity of liver detoxification enzymes such as the cytochrome P450 enzymes, which deactivates toxic chemicals and enables them to be safely excreted[11].

Hatcher H et al[29] conducted clinical trials on curcumin, where they studied the wide range of beneficial properties, including anti-inflammatory, antioxidant, chemo preventive and chemotherapeutic activity of curcumin. Curcumin is a free radical scavenger and hydrogen donor, and exhibits both pro- and antioxidant activity. It also binds metals, particularly iron and copper, and can function as an iron chelator. Curcumin is remarkably non-toxic and exhibits limited bioavailability. Curcumin exhibits great promise as a therapeutic agent, and is currently in human clinical trials for a variety of conditions, including multiple myeloma, pancreatic cancer, myelodysplastic syndromes, colon cancer, psoriasis and Alzheimer's disease.

Nitin Nigam et al[30] evaluated the efficacy of curcumin in reducing the burning sensation in potentially malignant disorders of oral cavity. 100 subjects were diagnosed clinically with potentially malignant disorders of oral cavity were included in this study. The patients were administered commercially available turmeric systemically and topical application of turmeric and honey was advised. Their burning sensation on VAS scale was evaluated after 15 days, and the data was then statistically analyzed by Wilcoxon sign rank test. After the treatment there was a significant decrease in VAS scale. The median showed decrease from 7 to 4. The mean value also showed decrease from 6.91 to 3.98.

In our study, tulsi and curcumin were used along with conventional treatment to increase the mouth opening and reduce burning sensation. When compared with the control group, the study group showed better results in terms of increased mouth opening and reduction in burning sensation.

4. CONCLUSION

The synergistic effect of tulsi and curcumin were evaluated in the management of OSMF along with conventional oral antioxidant therapy and the results were satisfactory in terms increasing mouth opening and reducing burning sensation. Large sample size and long term follow up studies are required to quantify the results and advantages of adding Tulsi and curcumin to the conventional therapies in management of OSMF.

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