

Effect of curcumin in management of potentially Malignant disorders-A comparative study

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SUMMARY

Aims and Objective: Oral Potentially Malignant Disorders (Pmds) are one of the most prevalent lesions worldwide today. Leukoplakia, lichen planus (LP) and Oral Submucous Fibrosis (OSMF) are the utmost common potentially malignant disorders, which if not treated, can be lethal. Turmeric and its active ingredient "curcumin" are being studied upon as chemopreventive agents in oral leukoplakia. Curcumin is the most active ingredient of turmeric and it exhibits antioxidant, anti-inflammatory, and pro-apoptotic activities. The purpose of the study was to evaluate and compare the efficacy and effect of curcumin in oral potentially malignant disorders in systemic form.

Materials and Methods: The present study was conducted in our institution. The sample size consisted of 60 patients who were clinical-histopathologically diagnosed with leukoplakia, lichen planus, and OSMF. The study group comprised of Group A-20 patients with Leukoplakia, Group B-20 patients with lichen planus and Group C-20 patients with OSMF. In all the three groups curcumin (cap Himalaya Haridra) 400 mg once daily was administered in systemic form for 3 months. Follow up was done up to 6 months. Data was statistically analyzed by SPSS 16, paired t-test and one tail unpaired t-tests were used.

Results: A significant increase in the mouth opening was observed in Group C and marked decrease in the size of lesions in groups A, B, and C.

Conclusion: Our study suggests that curcumin is a potent, safe and inexpensive modality for the management of PMDS

Key words: oral leukoplakia, curcumin, antioxidant, anti-inflammatory

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INTRODUCTION

The oral cavity is the sixth leading site for oral cancer worldwide [1]. Majority of Oral Squamous Cell Carcinomas (OSCC) evolve from PMDS [2]. Accurate diagnosis and appropriate management of premalignant disorders arrest the malignant transformation. In India majority of the oral cancers develop due to deleterious habits viz. tobacco chewing and smoking. Lack of knowledge of clinical presentation of PMDS amongst general practitioners postpones early diagnosis of these disorders [3, 4]. The World Health Organization defines PMDs as a lesion/condition which has a risk of transforming into malignancy either at initial or later diagnosis. Leukoplakia, erythroplakia, Lichen planus (LP), and Oral Submucous Fibrosis (OSMF) are the most commonly occurring PMDs and most likely to transform into malignancy [5, 6].

Leukoplakia, a potentially malignant disorder is a white patch or plaque that cannot be histologically or clinically distinguished as any other disease. Buccal mucosa, lip, and gingiva are more commonly involved. Lesions occurring in floor, tongue, and Vermilion area have a significant association with dysplastic changes, which is reported to be 15.6%-39.2% [7, 8]. OSMF may be defined as a slowly progressing disease in which the fibrous bands form in the oral mucosa, resulting in restricted mouth opening and tongue movements [9, 10]. The utmost frequency is found in South East Asians.

This condition has more predilection for males in the age group of 20-30 years. Clinical manifestations include buccal mucosa as the most frequently occurring site and severe trismus and burning sensation as the presenting complaint [1, 11].

Oral Lichen Planus (OLP) is a chronic inflammatory disorder, affecting the skin and mucous membrane. It has a high predilection for females. Common sites include buccal mucosa, gingiva, and tongue [12, 13].

Most of the PMDs are related to cigarette smoking, excess alcohol consumption, and betel nut chewing. Besides these, immunocompromised disorders and certain dietary factors are an independent threat to the progression of oral PMDs. Studies show that human papillomavirus (HPV)-16 and HPV-18 are associated with viral etiopathology of oral PMD. Since oral PMD have a high tendency to transform into malignancy, there is a need to identify these disorders early and prevent their transformation to malignancy by various means [14-16].

In the recent years, with the advancement in the field of medicine, antioxidants have earned a lot of importance because of their potential as prophylactic and therapeutic agents in potentially malignant disorders viz leukoplakia, lichen planus, etc. Plants derived antioxidants have been an essential seedbed of medicines worldwide. Turmeric has significant curative effects. Turmeric and its active ingredient, “curcumin” are being used as chemopreventive agents in India and abroad. Curcumin constrains various disorders due to their chemo-preventive and antineoplastic activity [17].

Curcumin a polyphenol originated from the herbal remedy and spice turmeric acquired wide-ranging anti-inflammatory and anticancer properties. It is not toxic to humans at doses up to 8000 mg/day [18, 19]. There are fewer studies done on the efficacy of curcumin in treating potentially malignant disorders so far.

MATERIALS AND METHODS

20 patients with oral leukoplakia, 20 patients with lichen planus and 20 patients of OSMF were considered for the potential study. All diagnostic tests were evaluated for diagnosing oral PMDs. Each subject completed a questionnaire to evaluate the prevalence of diseases, smoking, alcohol and drug history. Pain control and healing of lesions were 2 main clinical variables for evaluating cure of leukoplakia, lichen planus, and OSMF. To measure pain we used pain analog ranging from analog 0.5 (very mild) to 5 (severe pain). For healing, we measured the change in lesions size (five-point rating scale). For OSMF patients mouth opening was also taken into consideration.

Inclusion criteria

- Patients of either sex diagnosed as leukoplakia, lichen planus or OSMF
- Patients who are physically healthy and well oriented with time
- Patients who had not taken any treatment earlier for mentioned diseases
- Patients who are ready to quit smoking, tobacco and alcohol habits

Exclusion criteria

- Subjects with any systemic ailments
- Subjects with any pre-existing malignant disorders
- Expecting females
- History of hypersensitivity to curcumin (turmeric)

Informed consent was obtained from all the patients in the study group. Ethical clearance was pre-cured of the institutional council. Patients were divided into 3 groups; group A, group B and group C. Curcumin (Himalaya haridra) in systemic form was administered to the study population for a duration of three months. Each capsule contains 400 mg of curcumin. They are sealed in a plastic bottle containing 60 each. Patients were advised to consume one capsule once daily. Patients were mandated to visit every 15 days till three months of the treatment regimen. Follow up was done up to six months. There was marked clinical improvement in the size and symptoms of

potentially malignant disorders viz leukoplakia, lichen planus and OSMF in the present study (Figures 1-3). Clinical scores were filled in the proforma and data was examined. The mean values of the size of the lesions in three groups pre and post-treatment was calculated by student’s pair t-test. Mouth opening in Group C (OSMF) was analyzed pre and post-treatment using two-tailed unpaired t-tests.

RESULTS

All the patients in the study tolerated the treatment regimens well. Treatment was accepted by all the patients effectively without any side effects.

The study consisted of 60 patients who were divided into 3 groups. Group A consisted of 20 patients having oral leukoplakia. Group B consisted of 20 patients diagnosed with oral lichen planus and group C consisted of 20 patients with OSMF. The mean size of the lesion in group A before treatment was 4.05 with the standard deviation of 1.695 and was 1.292 after treatment with the standard deviation of 1.1043 (Table 1).



Fig. 1. Pre and post treatment curcumin in leukoplakia



Fig. 2. Pre and post treatment curcumin in lichen planus



Fig. 3. Improvement in OSMF post curcumin therapy

The mean difference in group A was 2.7570.

The mean size in group B before treatment was 4.20 before treatment with the standard deviation of 0.548 and was 0.82 after the treatment with the standard deviation of 0.406 (Table 2). The mean difference in group B was 3.375.

The mean size in group C before treatment was 3.89 before treatment with the standard deviation of 1.022 and was 1.974 after the treatment with the standard deviation of 0.6341 (Table 3). The mean difference in group B was 1.9211. The p-value is highly significant in all three groups (Graph 1).

It can be observed that there was a marked reduction in the size of lesions in all groups post-treatment curcumin therapy. There was a marked significant increase in the mouth opening in group C post curcumin therapy (Table 4). The pre-treatment mouth opening in group C was in the range of 12-28 mm, with a mean of 18.8 mm. After administration of curcumin for 3 months, there was a significant increase in mouth opening $p < 0.0001$ with a mean of 38.4 mm. No relapse was encountered at the follow-up. This study suggests that curcumin can be effectively used in treating PMDs.

DISCUSSION AND CONCLUSION

Role of Curcumin in potentially malignant disorders

Curcumin may suppress or prevent the oral pre-cancerous and cancerous lesions and condition by inhibiting free radical [20]. Curcumin is a potent chemopreventive agent, with remarkable antioxidant and therapeutic properties in various diseases viz cancer, diabetes. It acts as a free radicle scavenger of reactive oxygen and nitrogen species [20, 21].

This research was conducted in our Department on 60 patients of either sex diagnosed with PMDs. Patients who were in good physical condition and deemed fit for the study were taken.

In the present study, we took 60 patients who had not taken any treatment earlier. They were divided into 3 groups. All groups were given curcumin capsule 400 mg once a day. Our study showed highly significant results in all group. P value is less than 0.0001 which is highly significant. Similar research was done by Rai B et al. [4] in the year 2009 at Belgaum, Karnataka to evaluate the potency of curcumin in PMDs. The study group

Tab. 1. Pre and post-treatment mean score in leukoplakia

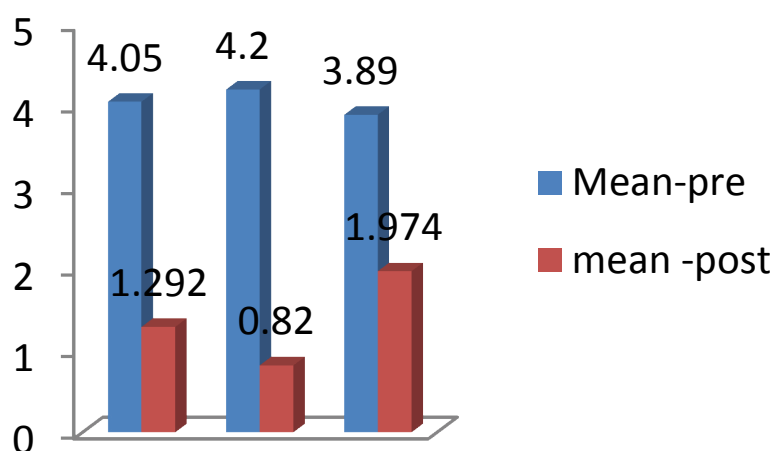
Group A	Mean	N	Std. deviation	Std. error mean	Mean difference	p-value
Pre	4.05	20	1.695	0.379	2.757	0
Post	1.292	20	1.1043	0.2469		

Tab. 2. Pre and post-treatment mean score in lichen planus

Group B	Mean	N	Std. Deviation	Std. error mean	Mean difference	p- value
Pre	4.2	20	0.548	0.122	3.375	0
Post	0.82	20	0.406	0.091		

Tab. 3. Pre and Post-treatment Mean score in OSMF

Group C	Mean	N	Std. Deviation	Std. error mean	Mean difference	p- value
Pre	3.89	20	1.022	0.234	1.9211	0
Post	1.974	20	0.6341	0.1455		



Graph 1. Graph depicting mean size pre and post-treatment in three groups

Tab. 4. Mouth opening evaluation in OSMF pre and post-treatment and post-treatment

Group C	Mean	N	Std. deviation	Std. error mean	t	df	p-value
Pre	18.86	20	5.22	1.39	10.2	26	0.0001
Post	38.43	20	4.93	1.32			

consisted of 75 patients that were divided into 3 groups viz Group A - Leukoplakia (25 patients), Group B- Lichen planus (25 patients) and Group C-OSMF (25 patients). They reported that a daily dose of 1gm of curcumin was more efficacious than 400mg. Curcumin improved the clinical symptoms and reduced the lesion size in all patients. The p-value is less than 0.5 which is statistically significant which is similar to our study. Shiv Kumar et al. [22] in 2016 conducted a study on 20 patients only in which comparison is done between lycopene and curcumin. the p-value is less than 0.0001 for both the groups which suggested that curcumin can be used for treating leukoplakia as p-value was also highly significant. In a previous study, they took only leukoplakia cases, but in our study we took leukoplakia, lichen planus and OSMF cases and curcumin showed the highly significant result in all three groups.

Lichen planus

Singh V et al. conducted a study of 10 patients who were histo-pathologically confirmed with oral lichen planus. Curcumin was administered twice daily in ointment form up to 3 months. Clinical improvement was observed in 9 patients at the end of 3 months. The results were in accordance with the

present study concluding the potency of curcumin in lichen planus [23].

Oral submucous fibrosis

To assess the efficacy of curcumin in OSMF patients, a study was conducted in 48 patients with histopathological confirmation. The study population consisted of three groups. Group A-Curcumin capsules, Group B-turmeric oil and Group C-placebo (control group). Results were observed after three months. The researcher observed a remarkable reduction of clinical manifestation of the condition, and the results were almost equal by use of either of the type of curcumin [17].

Curcumin is considered to be safe and non-toxic. Its role in treating cancer is very promising. Curcumin can be used to treat oral potentially malignant disorders like OSMF, Lichen Planus, and Leukoplakia. Curcumin shows optimal results in treating the lesions. There are visible changes in the reduction of the size of lesions and an increase in mouth opening in OSMF patients. It will be the most cost-effective method. Further studies with a larger population are needed to evaluate the potency and optimum dose of curcumin.

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