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EFFICACY OF CURCUMIN IN THE TREATMENT OF ORAL LEUKOPLAKIA- A PROSPECTIVE STUDY

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ABSTRACT

Aims and Objective: Oral potentially malignant disorders are one of the most ubiquitous lesions worldwide today. Leukoplakia is one of the most 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 study was to evaluate the efficacy of curcumin in oral leukoplakia in systemic form.
Materials and methods: Study was conducted in 60 patients diagnosed clinico-histopathologically with leukoplakia. Patients were divided into 2 groups. Group A is controlled group. Group Bwas given commercially available curcumin 400mg twice a day in systemic form (cap. Himalaya Haridra). The study subjects were followed up for three months, regularly at 15 days intervals, and the data was statistically evaluated by SPSS paired t tests. Results: A significant improvement is seen in terms of decrease in the size of lesion and cure of lesions in group B
Conclusion: The observed effect of curcumin suggests that it can be effectively and safely used for the management of oral leukoplakia.

INTRODUCTION

Oral cancer is the sixth commonest cancer in the world. The World Health Organization (WHO) has appraised that 90% of oral cancers in India among men were associated with chewing and smoking habits.[1]Leukoplakia, the most common potentially malignant disorder of the oral cavity has 60% chance of developing into oral squamous carcinoma. World Health Organization defined leukoplakia as "a white patch or plaque that cannot be characterized clinically or histologically as any other disease".[2]

Oral epithelial dysplasia is the most important prognostic indicator for determining the malignant transformation risk of leukoplakia. Homogenous leukoplakia is of low risk and they are considered the most common potential malignant disorder, suggesting a clinically significant rate of malignant transformation.[3]

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 a major source of medicine since ages in many part of the world. Turmeric has a number of medicinal properties. Turmeric and its active ingredient, "curcumin" are being used as chemopreventive agents in India and abroad. Curcumin have been found to constrain many disease processes through their anti-inflammatory, antioxidant and anticancer properties.[4]

Turmeric (haldi), a rhizome of Curcumalonga, is a flavourful yellow-orange spice. Components of tumeric are called curcuminoids, which constitute mainly curcumin (diferuloyl methane), demethoxycurcumin, and bisdemethoxycurcumin. 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.[5,6]

MATERIALS AND METHODS

The study was conducted in the Department of Oral Medicine and Radiology, Divya Jyoti College of dental sciences and research, Modinagar, U.P. for aperiod of 6 months. 60 patients who were clinically and histopathologically confirmed with leukoplakia were selected for the study.

Inclusion Criteria

1. Patients of either sex diagnosed clinically and histopathologically as leukoplakia
2. Patients who are physically healthy and well oriented with time.

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3. Patients who had not taken any treatment earlier for leukoplakia.
4. Patients who are ready to quit the smoking, tobacco and alcohol habits.
5. Patients who are willing to come for regular follow ups for 6 months duration.

Exclusion Criteria

1. Patients with leukoplakia co-existing systemic illnesses or any debilitating diseases.
2. Patients who are already diagnosed as cancer patients.
3. Patients with other mucosal lesions like osmf and malignant leisons.
4. Pregnancy and lactating mothers
5. History of hypersensitivity to curcumin (turmeric)

Patients were divided into two groups, group A and group B. Patients who had signed the informed consent on an approved format were included in the study. Clearance to conduct the study was obtained from the ethical committee.

Group A is given placebo. Group B is given curcumin capsules for 3 months. Curcumin capsules were obtained from Himalaya, trade name is Himalaya haridra. Each capsule contains 400mg of curcumin. They are sealed in a plastic bottle containing 60 each. The patients selected for study were instructed to take 1 capsule twice daily. The patients were instructed to report every 15 days for clinical evaluation and to collect the medication. Informed consent was taken from the patients before the study. The patients were called upon every 15 days for 3 months of treatment and then followed up, every month for 6 months. The severity of clinical signs and symptoms were entered as scores in the proforma. There was marked reduction in the size of the lesion post treatment in group B (Figure 1,2).The data collected were tabulated and analyzed. The equality of mean scores of the two groups was tested statistically using students paired t test. The differences in the scores at 15 days, 1 month, 3 months and 6 months were compared.

RESULTS

The study consisted of 52 males and 8 females. In group A, 25 were males and 5 were females. In group B, 27 were males and 3 were females (table 1).

Table 1 Distribution of study participants acc. to gender

Gender	Group A	Group B	Total
Male	25(83.3%)	27(90%)	52(86.6%)
Female	5(16.6%)	3(10%)	8(13.3%)
Total	30	30	60

Overall male were predominated. Both the groups were comparable in terms of age and gender (table 2).

Table 2 Age of patients

Age of patient	Group A	Group B
20-30 years	6	10
31-40 years	8	8
41-50	10	8
51-60	6	4

None of the patients reported with any toxic effects or allergy. The most common site involved was buccal mucosa in 27(45%) patients followed by 20 (33.3%) in retrocommisural area, 10 (16.6%) in lower lip and 3(5%) in hard palate (table 3). The mean size of the lesion before the commencement of the treatment was comparable.

Table 3 Location of lesions in oral cavity

Site	No.of patient
Lower lip	10(16.6%)
Buccal mucosa	27(45%)
Retrocommursial area	20(33.3%)
Hard palate	3(5%)
Total	60

The mean size of the lesion in group A was 3.090 while the group B mean size of the lesion was 4.3430 before treatment. The group A mean size of the lesion was 3.037,while the group B mean size of the lesion was 2.763 after treatment (table 4 and 5).

Table 4 Summary of pre-treatment and post-treatment size of lesion in cm^2 in group A

Variable	Mean	N	Std. Deviation	Std. Error Mean	Mean Diff	T value	Sig.
Pre treatment	3.09	30	1.137	.208	.060	1.459	.155
Post treatment	3.03	30	1.171	.214			

Table 5 Summary of pre-treatment and post-treatment size of lesion in cm^2 in group B

Variable	Mean	Std. Deviation	Std. Error Mean	Mean diff	T value	Sig.
Pre-treatment	4.34	2.133	.389	2.2213	8.386	0.000*
Post treatment	2.122	1.5512	.2832			

*significant

The p value of group A is 0.2024 which is non significant. The p value of group B is less than 0.0001 which is highly significant, which depicts a significant improvement of the lesion with curcumin. It can be noted that the size of the lesion is significantly reduced in group B, suggesting that curcumin can also be used for treating the leukoplakia. (table 6)

Table 6 Pair wise comparison of two groups (A, B) with respect to pre-treatment and post-treatment size of lesion in cm^2

Variable	Group	Mean	Std. Deviation	Std. Error Mean	Mean diff	T value	P value
Pre treatment	A	3.09	1.137	.208	-1.253	-2.840	.006
	B	4.34	2.133	.389			
Post treatment	A	3.03	1.171	.214	.908	2.560	.013
	B	2.12	1.551	.283			

Table 6 clinical improvement in lesions in both groups

Response	Group A	Group B
Complete 100%	O	5
Partial 75%	0	16
Stable 50%	0	9
Progression 25%	2	0

Figure 1 Lesion before curcumin therapy

Figure 2 Post-treatment after curcumin therapy

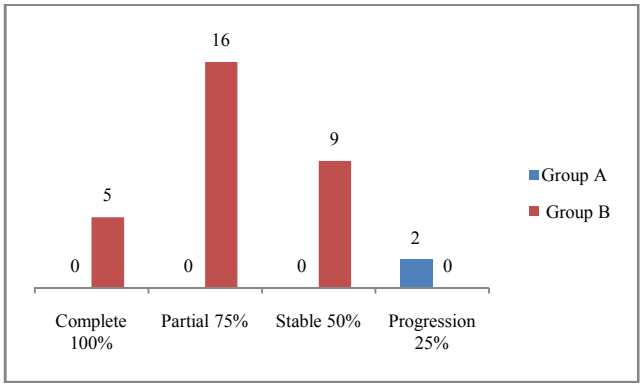

Figure 3 Clinical improvement in lesions in both groups

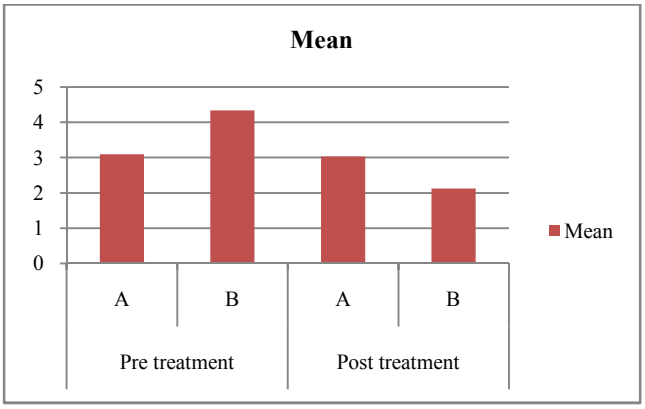

Figure 4 Graph representing comparison of pre-treatment and post-treatment size of lesion in cm^2 scores in two groups (A, B)

DISCUSSION

Curcumin may suppress or prevent the oral pre-cancerous and cancerous lesions and condition by inhibiting free radical.[7,8] They exhibit anti-neoplastic, anti-proliferative, and anti-mutagenic activities by subduing initiation, progression, and metastasis and interrupting cell cycle by disrupting mitotic structures and inducing apoptosis.[9]Curcumin reduces inflammation and it acts as an antimicrobial and a chemo-radiosensitizing agent and helps in wound healing apart from its antineoplastic properties.[10]It reduces inflammation by lowering histamine levels and possibly by increasing the production of natural cortisone by the adrenal glands. Oral administration of curcumin in instances of acute inflammation was found to be as effective as cortisone or phenylbutazone, and half as effective in cases of chronic inflammation.[11,12]

The present study was conducted in the Department of Oral Medicine & Radiology on 60 patients of either sex diagnosed clinically and histopathologically as leukoplakia. Patients were physically healthy and well oriented with time. In present study there were 52 males and 8 females. Similarly a study was conducted by Shiv Kumar *et al* in 2016, in which there were 13 males and 7 females with the male predominance as in the present study. Similarly one more study was done by Rai B *et al* in 2009 in which there were 13 males and 12 females with male predominance. We took large sample size as compared to both studies. There are fewer studies done on efficacy of curcumin in treating leukoplakia so far.

In the present study, we took 60 patients who had not taken any treatment earlier. They were divided into 2 groups. Group A was control group and group B was given curcumin capsule 400mg twice a day. Our study showed highly significant results in group B. p value is less than 0.0001 which is highly significant and in control group result is non-significant. (Figure 4)Similar study was conducted by Rai B *et al* in year 2009 at Belgaum, Karnataka for curcumin efficacy in precancerous lesions 25 patients each having leukoplakia, were given 1 g of curcumin tablets. 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. p value is less than 0.5 which is stastically significant which is in accordance with the present study.

Shiv kumar *et al* in 2016 conducted a study on 20 patients only in which comparision is done between lycopene and curcumin. p value is less than 0.0001 for both the groups which suggested that curcumin can be used for treating leukoplakia and the t test value of curcumin group at p level less than 0.0001 is 15.614 which showed there was a significant improvement in the lesions with curcumin therapy. The t test value of present study at p value lesser than 0.0001 is 8.3857 for curcumin group. This was also in accordance with present study. In present study the complete 100% clinical improvement was seen in 5 patients, partial improvement 75% was seen in 16 patients, stable 50% was seen in 9 patients and progression 25% was seen in none. Where as in study conducted by Shiv kumar *et al*, complete 100% clinical improvement was seen in 5 patients, partial improvement 75 % was seen in 3 patients, stable 50% seen in 2 patients and progression was seen in none.(Figure 3)

India produces nearly the whole of the world's turmeric crop and consumes 80% of it.[13]Curcumin is available in oral, intravenous, subcutaneous, and topical application in the form of gel, ointments, and nasal spray. There are certain limitations of using curcumin commercially like low solubility, prompt breakdown, and rapid elimination; hence, less than required bioavailability.

CONCLUSION

Curcumin is considered to be safe and non-toxic. Its role in treating the cancer is very promising. Curcumin can be used to treat oral potential malignant disorders like OSMF, Lichen Planus, Leukoplakia. Curcumin shows optimal results in treating the lesions. There are visible changes in the reduction of the size of lesions. It will be the most cost effective method. More researches are required to determine the optimal dosage, bioavailability, and bio-efficacy of curcumin-based drugs.

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