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Assessment Of Vitamin E, Melatonin And Bleomycin Efficacy In Management Of Oral Leukoplakia

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ABSTRACT

Aim: To assess the efficacy of Vitamin E, Melatonin and Bleomycin in leukoplakia management.

Materials & Methods: This observational prospective study comprised of 45 patients of oral leukoplakia and divided into 3 groups of 15 samples in each group. Group I patients were prescribed Vit E, Group II with Melatonin and Group III with Bleomycin. The clinical and

histological improvement was recorded till 6 months follow up. Collected data were statistically analyzed using SPSS software version 22. P value less than 0.05 was considered significant.

Results: Complete improvement of leukoplakia was seen in 3, 6 and 4 patients, in group I , II and group III respectively. Partial improvement was seen in 3,7 and 5 patients in group I ,II and group III respectively. Better clinical response was observed with Melatonin (Group I) followed by Bleomycin (Group II) and Vit E (Group II). In group I, for post treatment, 7 cases were normal, 5 cases had atypical hyperplasia, 3 had mild dysplasia and 1 were moderate dysplasia. In group II during post treatment, 13 were normal, 2 had atypical hyperplasia, 0 were mild dysplasia. In group III during post treatment, 9 were normal, 6 had atypical hyperplasia, 0 were mild dysplasia. Post treatment improvement in group I ($p>0.01$), and II ($p>0.4$) was statistically significant.

Conclusion: Authors found that Vit E, Bleomycin, and Melatonin are useful and effective in managing cases of oral leukoplakia.

Key words: Bleomycin, Leukoplakia, Melatonin, Vitamin E

INTRODUCTION

Oral leukoplakia (OL) is a premalignant lesion stated as "a predominant white lesion of the oral mucosa which cannot be defined as any other known lesion". [1, 2] Its prevalence in the general population varies from less than 1 - 5 %. There are 2 variants of leukoplakia ie, homogeneous and non-homogeneous. It is usually asymptomatic but can transfer to squamous cell carcinoma.[2] OL is most commonly found in older and elderly men, and its prevalence rises with age advancement. Its etiology is usually due to tobacco habit. OL located on the floor of the mouth, soft palate, and tongue is considered as high-risk lesions. [1]

Nonsurgical treatment may also be considered for the management of OL. This modality offers minimal adverse effects to patients. Various other modalities and medications are advised to treat leukoplakia such as; Photodynamic Therapy, Celecoxib, Beta-Carotene, Vitamins (A, C, E), Bleomycin, green tea and Curcumin. [1,2, 3]

Beta-carotene is a carotenoid commonly found in dark green, orange or yellowish vegetables, such as spinach, sweet potato, carrots, mango. α-Tocoferol (Vitamin E). α-Tocoferol (AT) is the common and most active form of vitamin E. Tocoferol is an effective antioxidant at high levels of oxygen.[1] Bleomycin, a cytotoxic antibiotic, was first used for the treatment of neoplasms. 0.5%/day topical Bleomycin is used for oral leukplaoka and as anti-neoplastic agents (1%).[1, 3] Antioxidants have been proposed to be useful in the chemoprevention and management of various precancerous lesions. Antioxidants are available as; Melatonin, Lycopene, Coenzyme q10, Vitamin A, beta carotene, Vit C, and Vit E. [4]

Melatonin (N-acetyl-5-methoxytryptamine) is antioxidative, immunomodulatory, protects cells during severe inflammatory processes and reduces oxidative damage. It is nontoxic highly

lipophilic indole, which make it possible for penetration through cell membranes. It inhibits human cancer cell growth. [5, 6]

There limited studies on efficacy of Vit E, Bleomycin, and Melatonin in managing cases of oral leukoplakia. Hence the present study was conducted to evaluate the efficacy of Vit E, Melatonin and Bleomycin in management of leukoplakia.

MATERIALS AND METHODOLOGY

This study was conducted in department of Oral Pathology after obtaining the approval from the institutional ethics committee. Participants informed approval was attained prior to study.

This prospective, study was conducted among 45 patients of oral leukoplakia which was confirmed by both clinically and histologically. The study sample was divided into 3 groups with 15 samples in each groups based on medicine used to treat leukoplakia; Group I patients were prescribed Vit E, Group II with Melatonin and Group III with Bleomycin. Inclusion criteria were confirmed cases of oral leukoplakia (homogenous, non- homogenous) in age range of 18- 60 years of both genders. Exclusion criteria were potentially malignant disorders except leukoplakia and those not giving consent for the study. Based on the calculated effect size of 0.83, 5% level of precision, 95% confidence level and 80% power of the study. The sample size for the study was 45 i.e 15 samples per group.

Patients were randomly divided based on lottery system into 3 groups. Group I patients were prescribed Vit E, Group II with Melatonin and Group III with Bleomycin. .

In all patients, size of the lesions, clinical improvement such as complete remission (100%), partial improvement (>50%), stable response (<50%)and progression ie. appearance of a new lesion was recorded. Patients were recalled regularly for assessment of the lesions for 6 months. Results were statistically evaluated using SPSS software version 21 with ANOVA test. P value less than 0.05 was considered significant.

RESULTS

Table 1 indicates clinical improvement of leukoplakia. Complete improvement was seen in 3, 6 and 4 patients, in group I , II and group III respectively. Partial improvement was seen in 3,7 and 5 patients in group I ,II and group III respectively. Stable response was in 9,2 and 6 patients in group I ,II and group III respectively. This indicate better clinical response observed with Melatonin (Group I) followed by Bleomycin (Group II) and Vit E(Group II). The changes were statistically significant.

Table 2 indicates histological improvement with leukoplakia patients. In group I, for post treatment, 7 cases were normal, 5 cases had atypical hyperplasia, 3 had mild dysplasia and 1 were moderate dysplasia. In group II during post treatment, 13 were normal, 2 had atypical hyperplasia, 0 were mild dysplasia. In group III during post treatment, 9 were normal, 6 had atypical

hyperplasia, 0 were mild dysplasia. Post treatment improvement in group I ($p>0.01$), and II ($p>0.4$) was statistically significant.

Discussion

Tobacco use, in any form, is counted as a major risk factor in the oral cancer development. Oral leukoplakia is associated with tobacco habit. The main purpose of early identification of leukoplakia is early interception and management to prevent its malignant transformation. [7]

The present study evaluated the efficacy of Vit E, Melatonin and Bleomycin in management of 45 leukoplakia patients.

Patel et al assessed the efficacy of lycopene in combination with vitamin E and selenium in the treatment of oral leukoplakia. They concluded that lycopene along with selenium and vitamin E in the management of oral leukoplakia.[7]

Kaur evaluated the combination of lycopene, beta-carotene and vitamin C in management of oral leukoplakia on 40 leukoplakia patients for a period of 6 months. They found that combination therapy was effective in management of leukoplakia compared to placebo group. [8]

It has been suggested that melatonin adjuvant therapy combined with conventional radio chemotherapy an excellent option for successful cancer treatment and oral precancerous conditions such as leukoplakia and lichen planus also respond positively to melatonin administration [9]

Epstein et al evaluated efficacy of topic bleomycin on 20 leukoplakia patients for 14 days and found reduction in size of lesions similar to our findings. [10]

Kaugars et al done a study on 79 patients with oral leukoplakia and they were received 30 mg of beta-carotene, 1000 mg of ascorbic acid, and 800 IU of alpha-tocopherol per day. They found clinical improvement of the oral lesion was noted in 55.7% of the patient after 9 months follow up. [11] Wong et al evaluated bleomycin as topical agent for the treatment of leukoplakia for 2 weeks. They found decrease in the thickness of all of the lesions clinically and sharp decrease in size in one lesion.[12] Hammersley et al evaluated 0.5 per cent (w/v) solution of bleomycin sulphate in dimethyl sulphoxide daily on 6 patients with oral leukoplakia. After 14 days of applications, they found white patch peeled off and the resultant raw surface epithelialised. [13]

The shortcoming of the study is small sample size. Long follow up and inclusion and comparison of different medications could have been proved useful.

Conclusion

Authors found that combination of lycopene, selenium and vitamin E is useful and effective in managing cases of oral leukoplakia. However, large scale studies are required to substantiate the results obtained in our study.

Conflict of interest: nil

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Legends for illustration

Tables and graphs

Table 1: Clinical improvement of leukoplakia

Clinical prognosis	Group I (Vit E)	Group II (Melatonin)	Group III (Bleomycin)
Complete improvement	3	6	4
Partial improvement	3	7	5
Stable response	9	2	6
Progression	0	0	0

Table 2: Histological improvement of leukoplakia

Histological staging	Group I (Vit E)		Group II (Melatonin)		Group III (Bleomycin)	
	Pre-treatment	Post-treatment	Pre-treatment	Post-treatment	Pre-treatment	Post-treatment
Normal	0	7	0	13	0	9
Atypical hyperplasia	11	5	7	2	12	6
Mild dysplasia	3	3	6	0	2	0
Moderate dysplasia	1	0	2	0	1	0
Severe dysplasia	0	0	0	0	0	0
P value	0.42		0.01*		0.04	