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Original Research

Comparative study on topical bleomycin and topical steroid in oral leukoplakia

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ABSTRACT:

Background: Oral leukoplakia is a premalignant lesion described as a predominant white lesion of the oral mucosa which cannot be defined as any other known lesion". **Aim:** The study was to compare topical bleomycin and topical steroid in the treatment of oral leukoplakia. **Material and methods:** The present study was conducted to compare topical bleomycin and topical steroid in the treatment of oral leukoplakia. Forty patients were identified with a diagnosis of leukoplakia and were enrolled in the study and divided into two groups. Group I was treated with topical bleomycin and Group II was treated with topical steroid. **Results:** In the present study group I patients were treated with bleomycin and Group II were treated with topical steroid. In group I speckled leukoplakia was present in 6 patients, homogenous leukoplakia in 12 patients, 2 patients had leukoplakia within no limits. In group II speckled leukoplakia was present in 5 patients, homogenous leukoplakia in 11 patients, 4 patients had leukoplakia within no limits. In group I mild dysplasia was present in 9 patients, moderate dysplasia was present in 4 patients, 7 patients had severe dysplasia. In group II mild dysplasia was present in 8 patients, moderate dysplasia was present in 3 patients, 9 patients had severe dysplasia. Patients after immediate treatment in Group I shows Homogenous leukoplakia in 13 patients, minimum leukplakia in 5 patients, 2 patients had leukoplakia within limits. In Group II Homogenous leukoplakia was present in 11 patients, minimum leukplakia in 4 patients, 5patients had leukoplakia within limits. In group I normal epithelium was present in 4 patients and benign hyperkeratosis in 16 patients. In group II normal epithelium was present in 2 patients and benign hyperkeratosis in 18 patients. **Conclusion:** Our study concluded that topical bleomycin was better than topical steroid in treating oral leukoplakia.

Key words: oral leukoplakia, steroid, bleomycin, mild dysplasia.

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INTRODUCTION:

Oral leukoplakia (OL) is a premalignant lesion described as "a predominant white lesion of the oral mucosa which cannot be defined as any other known lesion".[1] Oral lesions can be classified into four groups comprising of ulcerations, pigmentations, exophytic lesions, and red-white lesions.[2] Although white lesions constitute only 5% of oral pathoses, some of these lesions such as leukoplakia, lichen planus, and proliferative verrucous leukoplakia have malignant potential as high as 0.5–100%.[3] Over the years potentially malignant disorders like oral leukoplakia (OL) and oral erythroplakia (OE) are associated with dysplastic cellular changes and hence carry a risk of undergoing malignant transformation leading to oral cancer (OC).[4] Leukoplakia may represent histologic findings of epithelial hyperplasia, hyperorthokeratosis and hyperparakeratosis with or without epithelial dysplasia, or carcinoma. Dysplasia may be present in an area of leukoplakia in up to 16% of lesions, and up to 10% may be malignant at the time of initial examination.[5-10] In dysplastic leukoplakia, the risk of malignant transformation has been reported to be as high as 43%.[11,12] The bleomycin is glycopeptide-derived antibiotic isolated from streptomyces. The biological action of bleomycin is through a sequence-selective, metal-dependent oxidative cleavage of DNA and RNA in the presence of oxygen. It can mediate the oxidative degradation of all major classes of cellular RNAs and inhibition of DNA synthesis.[13] Glucocorticoids have potent anti-inflammatory actions, including the reduction in the number and function of various immune cells, such as T and B lymphocytes,

monocytes, neutrophils, and eosinophils, at sites of inflammation. Glucocorticoids decrease the production of cytokines, chemokines, and eicosanoids and enhances the production of macrophage migration inhibitory factor.[14] The aim of the present study was to compare topical bleomycin and topical steroid in the treatment of oral leukoplakia.

MATERIAL AND METHODS:

The present study was conducted to compare topical bleomycin and topical steroid in the treatment of oral leukoplakia. Before the commencement of the study ethical approval was taken from the Ethical committee of the institute and informed consent was obtained from the patients. Cases of Carcinoma In Situ, invasive Squamous Cell Carcinoma, and lesions identified as inflammatory in nature (e.g., lichen planus) were excluded from the study. Pregnant women or women of child-bearing age in whom contraception was not confirmed were also excluded from the study. Forty patients were identified with a diagnosis of leukoplakia and were enrolled in the study and divided into two groups. Group I was treated with topical bleomycin and Group II was treated with topical steroid. All patients had clinically visible leukoplakia. The duration of the lesion, smoking history and alcohol use, oral hygiene status, and dental status were recorded. Three-millimeter punch biopsies of identified lesions, guided by toluidine blue and Lugol's iodine application, were conducted. Pathologic diagnoses of dysplasia and histologic grading of the dysplastic lesions were required before entering into the study. The pathology was interpreted by a single pathologist in a blinded fashion. The treatment solutions prepared fresh, were applied to the involved area by soaking pledgets of cotton in the solution with continuous application to the area for 5 minutes, once daily for 14 consecutive days. After application, the solution was stored in a refrigerator. Patients were assessed weekly during treatment and at least once in the 3 months after treatment. Biopsies, guided by toluidine blue and Lugol's iodine were repeated at 4 weeks after treatment. Laboratory study was completed prior to treatment and 2 weeks after treatment, and included complete blood count, electrolytes, blood urea nitrogen, and serum creatinine. Complete response was defined as no clinical and histologic evidence of leukoplakia. Partial response was defined as a reduction in the severity of the clinical nature of the lesion and/or a reduction of the histologic grading of the dysplasia.

RESULTS:

In the present study group I patients were treated with bleomycin and Group II were treated with topical steroid. Before treatment in group I speckled leukoplakia was present in 6 patients, homogenous leukoplakia in 12 patients, 2 patients had leukoplakia within no limits. In group II speckled leukoplakia was present in 5 patients, homogenous leukoplakia in 11 patients, 4 patients had leukoplakia within no limits. In group I mild dysplasia was present in 9 patients, moderate dysplasia was present in 4 patients, 7 patients had severe dysplasia. In group II mild dysplasia was present in 8 patients, moderate dysplasia was present in 3 patients, 9 patients had severe dysplasia. Patients after immediate treatment in Group I shows Homogenous leukoplakia in 13 patients, minimum leukplakia in 5 patients, 2 patients had leukoplakia within limits. In Group II Homogenous leukoplakia was present in 11 patients, minimum leukplakia in 4 patients, 5patients had leukoplakia within limits. In group I normal epithelium was present in 4 patients and benign hyperkeratosis in 16 patients. In group II normal epithelium was present in 2 patients and benign hyperkeratosis in 18 patients.

Table 1: Patients characteristics pretreatment

Variables	N	
	Group I	Group II
Clinical findings		
Speckled leukoplakia	6	5
Homogenous leuloplakia	12	11
Not within limits	2	4
Histological findings		
Mild dysplasia	9	8
Moderate dysplasia	4	3
Severe dysplasia	7	9

Table 2: Patients characteristics immediate post treatment

Variables	N	
	Group I	Group II
Clinical findings		
Within limits	2	5
Homogenous leuloplakia	13	11
Minimum leukoplakia	5	4
Histological findings		
Normal epithelium	4	2
Benign hyperkeratosis	16	18

DISCUSSION:

Oral leukoplakia (OL) has been defined as a white patch or plaque that cannot be attributed to any clinically or histologically definite lesion.[15,16] The prevalence of OL is reported 2.6% among general population. Most lesions are seen above the age of 50 with men being more commonly affected; however, a slight predilection for women has been found in some studies.[17]

Bleomycin, a cytotoxic antibiotic, was first used for the treatment of neoplasms of the penis and scrotum, but has also been employed for squamous cell carcinoma of the head and neck region, oesophagus, and skin.[18]

Steroids have different effects on different tissues, which are dose dependent. The reason for varied effect of steroids lies in its mechanism of action.[19]

Warnakulasuriya et al. listed the overall risk factors for malignant transformation in leukoplakia as follows: female gender, long duration of leukoplakia, leukoplakia in nonsmokers (idiopathic leukoplakia), location on the tongue and/or floor of the mouth, nonhomogeneous type, presence of Candida albicans and presence of epithelial dysplasia.[20]

Malmstrom M et al. stated that clinically visible changes can be appreciated only three months after the application of bleomycin therapy but once the lesions disappear, the recurrence rate is less than the cases which have been treated surgically.[21]

Hammersley N et al. uses 0.5 per cent (w/v) solution of bleomycin sulphate in dimethyl sulphoxide was used for 12 to 15 days on six subjects. Significant clinical and histopathological improvements were observed.[22]

The use of topical 1% bleomycin in DMSO was evaluated for the treatment of dysplastic OL. Bleomycin was applied once daily for 14 consecutive days to lesions of the oral mucosa in 19 patients. It was well tolerated with minor mucosal reactions. Immediate posttreatment biopsies showed that 75% of patients had resolution of dysplasia. Ninety-four percent of the patients attained at least partial clinical resolution. After a mean follow-up period of 3.4 years, 31.6% of patients had no clinically visible lesions. In 2 patients (11%), malignant transformation occurred.[23]

CONCLUSION:

Our study concluded that topical bleomycin was better than topical steroid in treating oral leukoplakia.

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