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Original Article

Comparison of efficacy of topical retinoid with topical steroids in the treatment of oral lichen planus in a tertiary care hospital Quetta

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Abstract

Objective To compare the efficacy of topical retinoids with topical steroids in the treatment of oral lichen planus presented in tertiary care hospital Quetta.

Methods The study was designed and was conducted in Dermatology department Bolan Medical College Hospital/ Sandeman provincial hospital, Quetta. The approval of the study was taken from the institutional ethical review board. The duration of study was six months, from 15. June 2020 to 15 January 2021.

Results A total of 82 patients were selected through non-probability sampling. The patients were included after complete examination and history taking. Patients were either diagnosed clinically or lesional biopsy was taken. The patients were grouped into two groups, one was named Group R (for topical retinoids), and another was named Group S (for topical steroids). Data was analyzed using SPSS version 25. Post stratification T test was applied by taking P<0.05 as level of significance. The total number of patients was 82, all with clinical diagnosis of lichen planus. The average age of patients was 41.1± 9.4 years.

Conclusion The steroid group showed significantly low post treatment scores as compared to the Retinoid group; (2.7±0.8 vs. 4.2±0.8; P=0.000). In addition, the steroid group showed significantly low post treatment symptoms score as compared to retinoid group (2.6±1.0 vs. 5.9±1.1; P= 0.000). Topical steroid therapy is more effective as compared to topical retinoids in terms of signs and symptoms in patients of lichen planus.

Key words
Topical retinoids with topical steroids; Oral lichen planus; Randomized controlled trial; Post stratification T Test.

Introduction

Lichen planus (LP) is a chronic mucocutaneous disorder affecting oral and genital mucous membrane, skin, nails, and scalp. It affects 1-2% of the general population. Lichen Planus can develop in one or more mucosal and non-mucosal sites on the body. Women are most affected by lichen planus. The mean age in adults is 30-70 years old. The oral involvement is however more common in the older population, who are between 5th and 6th decade. The prevalence of oral lichen planus varies between 0.2-2.3% in the literature and it also represents 0.6% of all oral disease encountered by dentists. It typically affects the mouth but can also be found on the lips and esophagus. It is estimated that the overall prevalence of oral Lichen Planus is between 0.5–1.5% but it is uncertain. Meanwhile oral mucosal involvement in systemic lichen planus patients is 70–77%.

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The exact incidence and prevalence are not known. Kaposi in a study conducted in 1895 reported 25-30 cases annually.[1] However, in our region of the Indian subcontinent it has a high incidence.[2] The relative risk seem to be highest (13.7%) in those who chewed and smoked tobacco, 3.7% in those with mixed oral habits and the lowest in non-tobacco consumers 0.3%.

Oral lichen planus has variable presentation, which appear as multiple, symmetrical lesions that may be reticular or have a lace like pattern. Lesions can be asymptomatic. Other types are plaque-like, papular, atrophic, erosive, or vesiculobullous forms. The reticular form is the commonest form. The erosive and atrophic forms are associated with burning pain exacerbated by hot and spicy food. Oral involvement can be the only sign of lichen planus, or it can be associated with lichen planus on other body sites. In case of presentation, thorough evaluation of other mucosal sites, nails and extensors of skin is important. The oral cavity can be involved extensively, leading to esophageal lichen planus and can lead to strictures, dysphagia, and also squamous cell carcinoma. The associations of oral lichen planus vary from region to region and the most established association include Hepatitis C, Human papilloma virus infections. The HCV infection is mostly asymptomatic with no liver involvement. But in about 20-30% it can lead to cirrhosis of liver in 20 years and has higher incidence of hepatocellular carcinoma. In OLP patients HCV is suggested to be an etiological factor.[3] Other diseases such as diabetes mellitus, hypertension, hypercholesterolemia are more related to lichen planus in general rather than OLP.

After history taking and clinical examination a diagnosis can be established. However oral lichen planus has several other differential diagnoses such as pemphigus vulgaris, mucus membrane pemphigoid, lichenoid drug eruptions, amalgam reactions, graft-versus-host disease. In case of any suspicion of other disease or where complications of OLP are suspected a lesional biopsy is sent for histopathological evaluation and confirmation. Moreover, in certain conditions where histopathological changes cannot distinguish OLP, immunofluorescence is helpful.

The treatment of oral lichen planus can include topical and systemic drug treatment, phototherapy, laser, and surgical options. Mostly targeted topical treatments are used such as corticosteroids, retinoids and immunosuppressives. The main aim is to resolve signs and symptoms and prevent cancers. The first line of treatment is high potency topical steroid until clinical remission. In case of no improvement oral corticosteroids are used or other treatment options are availed. The effects of steroids in reducing inflammation and inhibiting the migration and accumulation of inflammatory cells makes it the most widely used treatment modality. Different strengths are selected based on the severity of the lesions in patients. The other topical treatment that shows considerable effect are retinoid s which inhibit nuclear receptors (RAR-α, RAR-β, RAR-γ) and upregulate transcription. The epithelial cells are also regulated by retinoids and hence they have a role in suppressing neoplasia. These two drugs were selected for the study taking in consideration the effectiveness and easy availability in the region.

Methods

The cross-sectional non-probability sampling was done in the dermatology departments of Bolan medical complex hospital/ Sandeman provincial hospital, Quetta. The study was carried out for 6 months.

The sample size is calculated by using WHO sample size calculator as shown in **Table 1**.

Table 1 Sample size calculated by using who sample size.

Level of significance:	5%
Power of test:	80%
Population standard deviation:	0.48[11]
Test Value of the Population Mean:	0.4[11]
Anticipated Population Mean:	0.7 [11]

Sample size was n=82 total patients: 41 patients in each group.

The treatment outcome was recorded after three months in both group of patients, in terms of sign and symptoms scores. Symptoms such as pain and a burning sensation in the oral cavity was scored as:[4] 0- (no symptoms); 1- mild (occasional symptoms); 2- moderate (while eating spicy food); 3- severe (i.e., while eating any food); 4- intolerable (always present).

Signs were scored as:[5] 0- (no lesion present); 1- (only white striae present), 2- (white striae plus erosion of less than 1 cm^2); 3- (white striae plus erosion of more than 1 cm^2); 4- (white striae plus ulceration of less than 1 cm^2); 5- (white striae plus ulceration of more than 1 cm^2).

Patients were selected from the outpatient department of Sandeman provincial hospital, Quetta. An informed consent was obtained from patients before including them in this study and using their data. A thorough history taking and extensive examination was done to evaluate patients' inclusion and exclusion criteria. Biopsy of the patients was also taken in case of suspicion and sent for histopathology in the hospital laboratory to aid in diagnosis. The associations of lichen planus were ruled out.

The following inclusion and exclusion criteria were taken in consideration:

Inclusion criteria

- Diagnosed cases of oral lichen planus.
- Patients between age group 18-65.
- Both males and females.

Exclusion criteria

- Patients with hypersensitivity to any of the treatment drugs to avoid any pharmacologic reaction.
- Patient with any history of chronic kidney disease or chronic liver disease were excluded to avoid result bias and to minimize the risk of losing patients to follow up.
- Pregnant and lactating patients were excluded as to avoid steroid therapy in these conditions.
- All suspected lesions showing malignant and dysplastic changes were excluded to establish a more effective study.

Results

The demographic statistics on the base of age, gender, interventional groups, and type of OLP are as taken into consideration which are shown in **Figures 1-4** respectively.

Table 2 demonstrates the results comparing the baseline and post treatment sign scores.

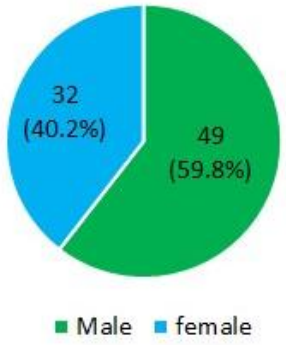

Figure 1 The demographic statistics based on gender.

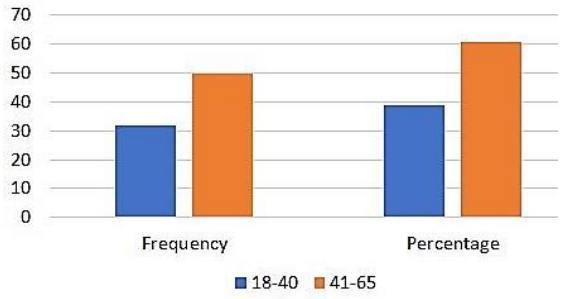

Figure 2 The demographic statistics based on age.

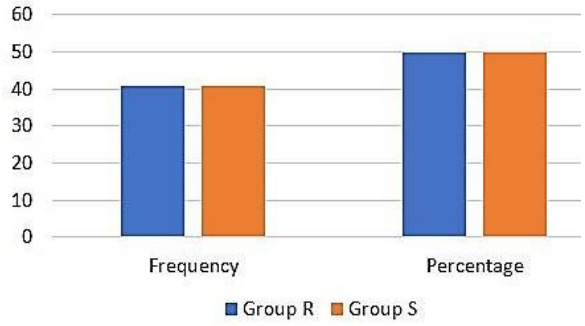

Figure 3 The demographic statistics based on Interventional groups.

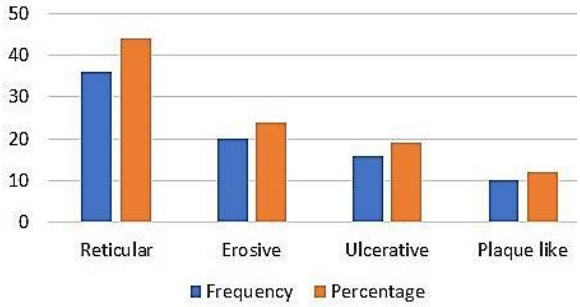

Figure 4 The demographic statistics based on types of OLP.

Table 2 A comparison of baseline and post treatment sign scores.

Sign scores/ groups	*N*	*Mean±SD*	*P value*
Baseline			
Group R	41	5.9±0.8	0.06
Group S	41	6.0±0.7	
Post treatment			
Group R	41	4.2±0.8	0.000
Group S	41	2.7±0.8	

Table 3 A comparison of baseline and post treatment symptom scores.

Symptoms scores/ groups	*N*	*Mean±SD*	*P value*
Baseline			
Group R	41	7.0±1.1	0.07
Group S	41	7.4±0.9	
Post treatment			
Group R	41	5.9±1.1	0.000
Group S	41	2.6±1.0	

Table 3 demonstrates the results comparing the baseline and post treatment symptom scores. There is significant change in baseline sign and symptom score in patients treated with steroid in OLP. The results were consistent in gender and age-group, however topical steroid application demonstrated lower scores.

There was no significance difference in the change in baseline signs and symptoms score with respect to type of OLP in both groups as shown in the following **Tables 4, 5**.

Discussion

Oral lichen planus is a chronic inflammatory skin condition. It is an autoimmune disease caused by the abnormal differentiation of basal keratinocytes. Most cases are idiopathic, but some factors can cause aggravation, such as drugs, dental dentures, viral infections etc. The patients commonly present with white lacy appearance in buccal mucosa or with pain and burning while eating in cases of erosive oral lichen planus. The chronic infiltration of the T-cells corresponds to chronic cellular infiltration.

The results of the current study show that topical steroid (0.1% Triamcinolone acetonide) was more effective and post treatment symptoms scores were lower as compared to topical retinoids (0.01% isotretinoin gel), (2.6±1.0 vs. 5.9±1.1; P=0.000). Pinus *et al.* conducted a study in Spain, where the role of corticosteroid (0.1% triamcinolone acetonide) in orabase was studied in oral lichen planus. In this study questionaries were distributed to dermatologists, maxillofacial surgeons, and dentists. In a scale of 1–10 the effectiveness was 6.68 (SD=2.26).[6]

Shetty *et al.* studied the effect of hyaluronic acid 0.2% (HA) as in treatment of oral lichen planus in comparison to placebo. This study was done to find an alternative to immunosuppressants for OLP.50 patients were selected who were symptomatic and had the diagnosis confirmed by biopsy. They were divided in two groups each consisted of 25 patients. One group was treated with HA 0.2% and the other group was treated with placebo for 14 days. The patient

Table 4 Stratification of baseline and post treatment sign scores with respect to OLP type.

	Sign score (Mean±SD)		
OLP type	*Baseline (N=41)*	*Post treatment (N=41)*	*P value*
Group R			
Reticular	5.5±2.1	5.4±2.0	0.546
Erosive	5.3±2.0	5.1±1.8	
Ulcerative	6.7±3.5	6.4±3.2	
Plaque like	6.6±3.1	6.1±3.0	
Group S			
Reticular	5.1±2.0	4.7±1.9	0.589
Erosive	7.6±4.1	6.7±3.9	
Ulcerative	5.7±2.9	5.3±2.4	
Plaque like	6.4±3.2	5.9±3.0	

Table 5 Stratification of baseline and post treatment symptom score with respect to OLP type.

	Symptoms score (Mean±SD)		
OLP type	*Baseline (N=41)*	*Post treatment (N=41)*	*P value*
Group R			
Reticular	5.7±2.1	5.6±2.0	0.921
Erosive	6.7±3.2	5.1±1.8	
Ulcerative	6.5±3.4	6.3±3.1	
Plaque like	6.4±3.1	5.9±2.9	
Group S			
Reticular	4.9±2.0	4.8±1.9	0.371
Erosive	7.5±4.1	6.7±3.9	
Ulcerative	4.9±2.1	4.3±1.8	
Plaque like	6.4±3.2	5.9±3.0	

treated with HA 0.2% had significant reduction in signs and symptoms such as erythema and size of lesion.

Hyaluronic acid can have potential effect on OLP if more studies are done.[7]

In this study no significant difference was seen in baseline sign score and after treatment sign scores of patients treated with retinoid and the patients treated with steroid in regards to type of oral lichen planus (p=0.546; p=0.589 respectively). In a study conducted by Mostafa *et al.* on 66 patients of diagnosed OLP, the results of topical ozone to topical ozone and steroid therapy versus topical steroid as control in management of Atrophic- erosive LP were observed. The combination group showed significant improvement in sign scores and pain.[8]

The steroid use has its own limitations such as resistance to steroids, intolerance or prolonged use leading to candidiasis warranting anti-fungal therapy must be considered. While using super potent steroid for longer period can led to potential tachyphylaxis an adrenal insufficiency. In these patients retinoid can be considered as an alternative. In a study in 23 patients by Sloberg *et al.*,[9] the retinoid use showed significant results. In this study, comparison was done between 0.1% topical tretinoin and a placebo. There was marked improvement in patients. He repeated the same study four years later in 25 patients of oral lichen planus. The results were the same as the first study. In a study of 17 patients by Gunther[10] has shown that after three weeks of treatment with topical retinoids the size of oral lichen planus reduced. However, the cases relapsed, and histopathology showed no changes in metabolism of cells.

In a study by Karl *et al.*[11] topical tretinoin 0.05% was compared with topical betamethasone dipropionate 0.05%. It showed better results with tretinoin 0.05%. Further studies show different strengths of topical treatment are needed. In another study by Buajeeb *et al.*[12] comparison was done between 0.05% retinoic acid in orabase with fluocinolone acetonide 0.1% in orabase. The results favored 0.1% fluocinolone acetonide as being more effective in preventing cancer as a complication of oral lichen planus.

Scardina *et al.*[13] conducted the largest cohort study in 70 patients of oral lichen planus. In this study two different strengths of isotretinoin were compared i.e. (0.18% and 0.05%). In follow up, no improvement was seen in patients of reticular lichen planus. However, the effect of retinoids

on epithelial cells has an additional effect on dysplastic cells and in erosive lichen planus showed significant improvement. 0.18% cases also showed disappearance of dysplastic changes in oral lichen planus.

Conclusion

In this study, topical steroid therapy (0.1% triamcinolone acetonide in oral paste) was more effective as compared to topical retinoid therapy (0.01% isotretinoin gel) in patients of OLP in terms of symptom and sign scores. The data is very supportive of these outcomes. However, larger cohorts with randomized control trials and follow ups for longer period are warranted.

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