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Original Article

Evaluation of efficacy of a bioresorbable membrane in the treatment of oral lichen planus

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ABSTRACT

Background: Gingival involvement is commonly seen in lichen planus, a chronic mucocutaneous inflammatory condition of the stratified squamous epithelia. It is often painful and may undergo malignant transformation and thus warrants early diagnosis and prompt treatment. The aim of this study is to evaluate the use of a bioresorbable membrane (Polyglactin 910) in the management of erosive lichen planus of gingiva.

Materials and Methods: A split-mouth randomized controlled trial was carried out. Fifteen patients with identical bilateral lesions of lichen planus on gingiva were included in the study. Three parameters were selected for the clinical assessment of gingival lesions: Surface texture, color, and burning sensation. After complete oral prophylaxis, an excisional biopsy procedure was carried out for lesions on both sides, but on the experimental side, the biopsy procedure was combined with placement of the bioresorbable membrane. The statistical significance of intergroup differences in measurements was tested by using an independent sample *t*-test. A two-tailed *P*-value less than 0.05 was considered as statistically significant.

Results: Intragroup comparisons revealed a statistically significant difference between mean value of grades at 6, 12, and 24 weeks in both groups for the surface texture, color, and burning sensation of gingiva, respectively. For intergroup comparison of change in surface texture, color, and burning sensation of gingiva between group A and group B, differences were statistically nonsignificant.

Conclusion: Surgical management of the lesion accomplished significant improvement of lesion with no significant additional clinical benefits with the application of bioresorbable membrane. Worsening of baseline scores was not observed in any case at the end of the study.

Key Words: Bioresorbable membrane, excisional biopsy, gingiva, lichen planus

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INTRODUCTION

Lichen planus is a chronic inflammatory mucocutaneous disease, which frequently involves the oral mucosa. In the majority of patients with oral lichen planus (OLP), there is no associated cutaneous lichen planus or lichen planus at other mucosal sites. This may be called "isolated" OLP. OLP was first described clinically by Wilson in 1869 as a chronic mucocutaneous disorder.[1] Fifty percent of patients with skin lesions also manifest oral mucosal lesions, and 25% of patients with OLP present only oral lesions.[2] OLP most commonly occurs in middle-aged adults. Large retrospective studies from Europe and the United States indicate that the average age of patients presenting with OLP is around 50-60 years.[2-8] OLP is rare in children. Population-based studies performed in Asia, Europe, North America, and the Middle East have revealed disease prevalence rates between less than 1% and 3%[9,10] and more recently reported as 6.03%.[2]

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Current data suggest that OLP is a T cell-mediated autoimmune disease in which autocytotoxic CD8+ T cells trigger apoptosis of oral epithelial cells.[11] The characteristic clinical aspects of OLP may be sufficient to make a correct diagnosis if there are classic skin lesions present. An oral biopsy with histopathologic study is recommended to confirm the clinical diagnosis and mainly to exclude dysplasia and malignancy.[12] Histopathologic examination typically shows orthokeratotic hyperkeratosis, basal cell degeneration, and a dense well-defined infiltrate of lymphocytes in the superficial dermis. OLP lesions may result from the induction of keratinocytes apoptosis by cytotoxic CD8+ T cells stimulated by a yet unidentified self-antigen on a genetically predisposed patient.[7,13-16]

Clinically, manifestations generally occurs chronically, focally, or distributed over several areas with varying degrees of severity. The clinical features of OLP in the oral mucosa are generally polymorphic and usually consist of bilateral and/or multiple symmetric lesions, with manifestation of associated clinical patterns. Alternation between phases of exacerbation and quiescence has been reported. According to Andreasen,[3] OLP is classically divided into six forms: reticular, plaque-like, papular, atrophic, erosive, and bullous. The reticular form is the most common, followed by the erosive form.[2-7,17] OLP is most frequently observed on the buccal mucosa and vestibular areas and next frequently on the lateral regions of the tongue and gingiva.[16] Such lesions are confronted in routine by the dentist especially the periodontist.

The clinical differential diagnosis include lichenoid drug eruptions, lichenoid lesions associated with contact hypersensitivity to restorative materials, leukoplakia, lupus erythematosus, and graft versus host disease.[15] The etiology of OLP remains unclear. Different factors have been implicated in etiology of lichen planus such as diabetes mellitus,[14,15,18-20] thyroid disease especially hypothyroidism,[21] rheumatic collagen diseases,[20] allergy,[22] chronic stress syndrome,[20,11,22-24] hypertension,[18,20] infections (viral,[13,20,22,25,26] bacterial[3,22,27] (*H. Pylori* infection),[1] fungal[22,28,29]), HLA predispositions,[17,18,23] idiosyncratic drug reactions,[18,19,23,30,31] graft versus host reaction,[32,33] and local dental irritants.[3,22] The -308 G/A polymorphism may be a risk factor for OLP patients without HCV infection and those with mixed ethnicity. More studies are needed to validate these associations.[34]

Gingival involvement with lesions of lichen planus is a common occurrence.[35] In about 10% of patients with OLP, the lesions are confined to the gingiva alone sometimes making the diagnosis more difficult.[14] Twenty percent of the total cases of lichen planus have been reported to have gingival involvement by Jandinski and Shklar.[35] In a study by Mignogna *et al.*, 48% of patients of lichen planus suffered from gingival lesions.[36] Symptoms in OLP patients with gingival involvement may vary from mild discomfort to severe oral pain, with the general trend increasing from the keratotic to the erosive forms. Furthermore, the variable clinical appearance and the lack of symptoms may lead to a confusion of the diagnostic pattern and to unawareness of the disease by the patient.[36] Since gingival involvement in OLP has a high incidence, its recognition during routinely performed periodontal procedures could help both to reduce undiagnosed or misdiagnosed cases and to establish appropriate management.[14] From the oral point of view, it is well known that local factors such as dental plaque and calculus cause gingival OLP to worsen, resulting in erosive disease; in turn, the induced or enhanced severity of symptoms can interfere with the correct performance of daily oral hygiene, leading to increased deposits of these irritating factors.[36] The erosive and atrophic types most frequently undergo malignant transformation.[37] The best evidence currently available on the potentially malignant nature of OLP is from follow-up studies and retrospective incidence studies. The frequency of oral cancer among OLP patients moves in a relatively narrow range (0-5.3%) and do not contrast with those from prospective studies.[8,38] All these features warrant early recognition and management of such lesions.

Various treatment modalities have been tried from time to time.[1,14] These include griseofulvin therapy,[39,40] etretinate (75 mg/day),[23] topical cyclosporine therapy,[41] topical aqueous triamcinolone acetonide suspension,[20] topical application of 0.025% flucinonide,[42] cryosurgery,[43] electrosurgery,[44] free gingival graft,[45] laser systems — diode laser (980 nm),[46] and topical photodynamic therapy (PDT) mediated by methylene blue (MB-PDT).[47]

The literature is still not sufficient as regards to the treatment regimen of erosive lichen planus. Continuously new treatment methodologies keep on evolving for the diseases for which permanent treatment is not known. Bioresorbable membranes have been used successfully for the regeneration

of periodontal structures. According to Minabe,[48] biodegradable polymers may be best suited to support healing of damaged biological tissues by providing an appropriate scaffold or guidance. To best of our knowledge, this was the first investigation planned to evaluate the use of bioresorbable membrane (Polyglactin 910) in the management of erosive lichen planus of gingiva.

MATERIALS AND METHODS

Fifteen patients presenting the signs and symptoms of lichen planus with similar isolated/solitary bilateral lesions only on gingiva, between 30 and 60 years of age and capable of maintaining proper oral hygiene were selected from the outpatient department, Punjab Government Dental College and Hospital, Amritsar. Subjects with the presence of any systemic disorders and on medication, oral lichenoid drug eruptions, contact lichenoid lesions associated with restorative materials, chronic smokers, and alcoholics were excluded after a thorough history and complete clinical examination from the study. The study protocol was approved by institutional ethical committee. The selected study subjects were explained about the purpose and course of the study and asked for the voluntary participation in the study. The subjects were enrolled after signing an informed written consent for the participation.

Three parameters were selected for the assessment of gingival lesions. Subjective and objective evaluation was done based on arbitrary numeric scales according to the patient's response and observation by an examiner.

Surface texture

Surface texture of gingiva at the site of lesion was noted and graded according to the following scale:

0: Clinically healthy gingiva
1: Smooth (due to erosion)
or
Rough (due to hyperkeratinization)
or
Combination of smooth and rough

Color

The gingival color on the lesion site was noted and graded according to the following scale:

0: Pink/correlating with cutaneous pigmentation
1: Reddish pink
2: Red
3: Dark red

Burning sensation

Patients were asked to rate the burning sensation to hot, salty and spicy food, and toothpaste at the site of the lesion on the following scale:

0: Absent
1: Mild
2: Moderate
3: Severe

A bioresorbable membrane, vicryl mesh was used in this study, which is composed of undyed fibers of polyglactin 910, the same copolymer as vicryl sutures that have a long history of safe use in humans since 1974. It is a synthetic bioresorbable copolymer of glycolide and lactide, derived from glycolic and lactic acids, which are natural metabolic acids readily eliminated from the body. Polyglactin 910 is nonantigenic, nonpyrogenic and elicits only mild tissue reaction during resorption [Figure 1].

Method

The study was carried out using split mouth study design. The bilateral lesions, in each individual, included were divided into two groups

- Group A (lesion on the right side was kept as experimental): In this group, the excisional biopsy procedure was combined with placement of the bioresorbable membrane.
- Group B (lesion on the left side was kept as control): In this group, a similar excisional biopsy procedure was carried out without the placement of the bioresorbable membrane.

Full mouth scaling and root planing and occlusal equilibration for every case were carried out, and

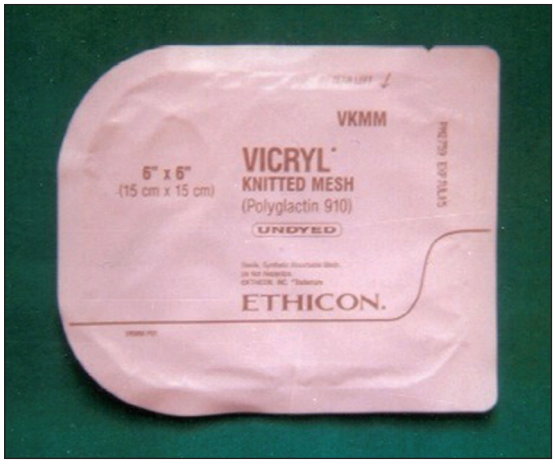

Figure 1: Bioresorbable membrane (vicryl knitted mesh polyglactin 910) used in the study

the patient was instructed to adopt meticulous oral hygiene measures to control the dental plaque. Routine laboratory investigations including Hb, BT, CT, TLC, DLC, fasting sugar level, and complete routine urine examination were carried out.

All the patients were operated upon under local anesthesia using xylocaine 2% with adrenaline (1:80,000).

Group A (Experimental)

An infiltration anesthesia was given around the lesion. Excisional biopsy was performed, including 1-2 mm of healthy gingiva around the lesion with a sterile BP blade no.11 [Figures 2-4]. The tissue was resected up to the periosteum so as to free the periosteum of all submucosal tissue. The excised tissue was taken out with tissue forceps, kept in 10% formalin and sent for histopathological examination. The bioresorbable (polyglactin 910) membrane was cut according to the size of the excised tissue and placed on the wound area. Interrupted sutures were given with bioresorbable sutures (Vicryl 4-0).

Group B (Control)

For Group B, the same procedure was carried out as in Group A except for the placement of the bioresorbable membrane [Figures 5 and 6]. Postoperative instructions were given and the patients were asked to report after 7 days for check up and immediately in the case of pain or any other discomfort.

The patients were recalled after 6, 12, and 24 weeks period from baseline, keeping healing of the surgical wound, in view. At each recall, the lesion was examined for surface texture, color, and burning sensation and graded on an arbitrary numeric scale prepared for the study [Figures 7-10].

Statistical analysis

Mean and standard deviation for all parameters were calculated. The statistical significance of

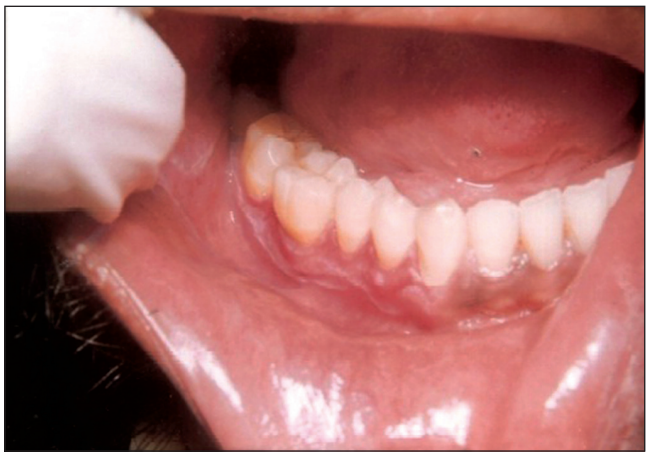

Figure 2: Preoperative view of lesion on the right side (Group A)

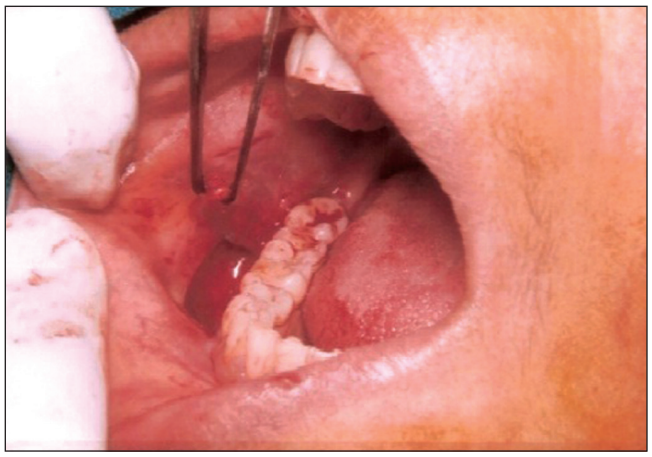

Figure 3: Resected tissue on the right side (Group A)

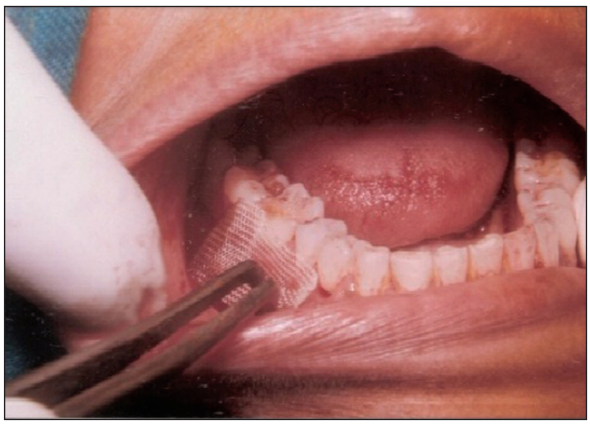

Figure 4: Bioresorbable (polyglactin 910) membrane being placed on the prepared wound (Group A)

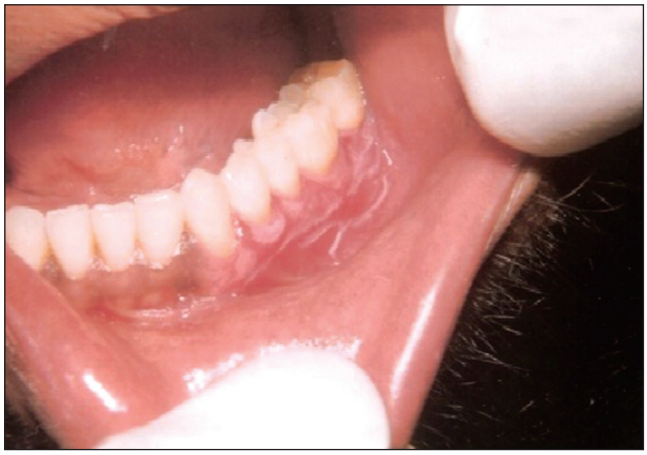

Figure 5: Preoperative view of lesion on the left side (Group B)

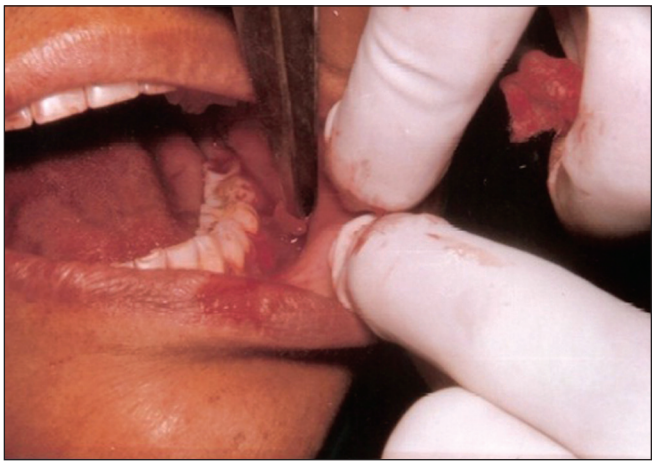

Figure 6: Resected tissue on the right side (Group B)

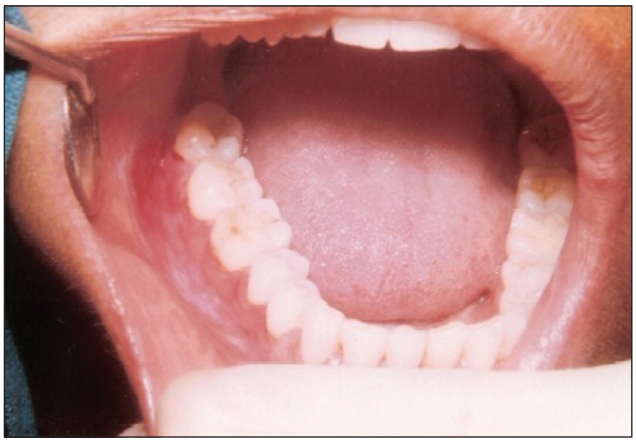

Figure 7: Postoperative view of the area on the right side (Group A) at 6 weeks of observation

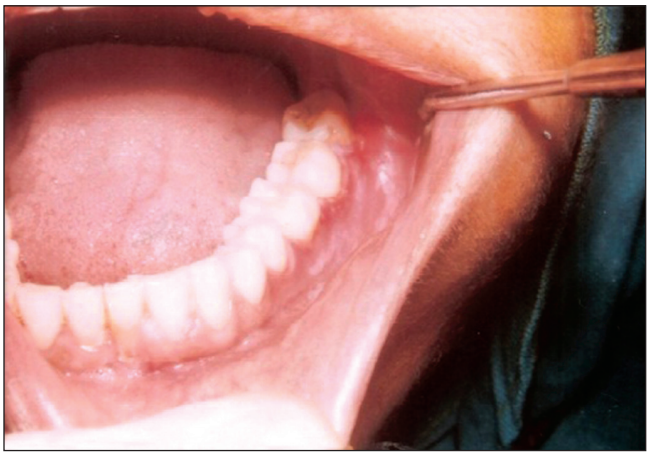

Figure 8: Postoperative view of the area on the left side (Group B) at 6 weeks of observation

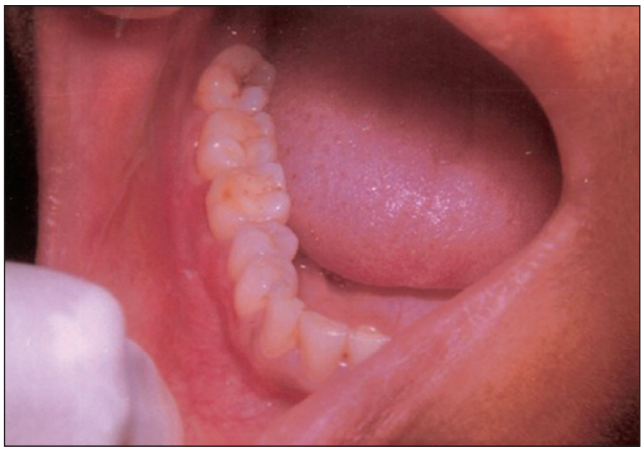

Figure 9: Postoperative view of the area on the right side (Group A) at 24 weeks of observation

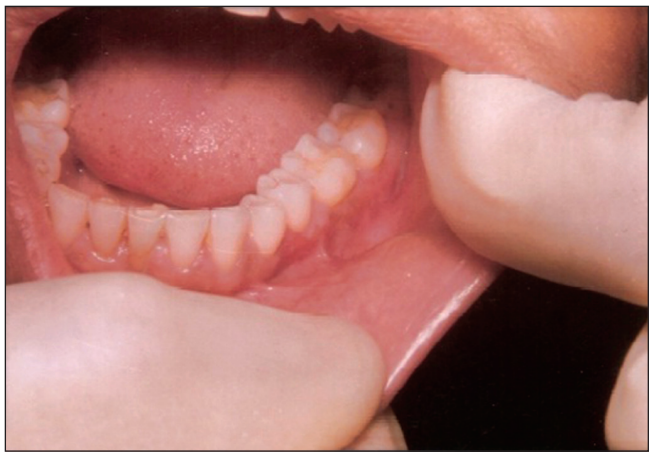

Figure 10: Postoperative view of the area on the left side (Group B) at 24 weeks of observation

differences in independent variables for the intragroup measurements were analyzed by using the Student *t*-test (two-tailed, paired). The statistical significance of intergroup differences in measurements was tested by using independent samples *t*-test. A two-tailed *P*-value less than 0.05 was considered as statistically significant.

RESULTS

The mean age for study population was 35 ± 5.62 years and the study population consisted of six males and nine females. Table 1 shows mean value of response for surface texture, burning sensation, and color of gingiva at the different periods of observation. Table 2 shows mean reduction in scores of clinical parameters in both groups over a period of 24 weeks. The mean value of grades for surface texture of gingiva, color of gingiva, and burning sensation of gingiva in both groups reduced from 1 to 0.2, 2.8 to 1.47 and 2.93 to 1.84, respectively, over an observation period of 24 weeks.

Table 3 depicts the mean value of grades at different periods of observation in both the groups for surface texture, color, and burning sensation of gingiva. Statistically significant intragroup differences were observed for all the parameters at different periods of observation in both the groups. The differences for mean change in grades for surface texture, color, and burning sensation of gingiva between group A and group B were statistically nonsignificant.

In this study, the following histopathological changes were observed: Hyperkeratinization of the epithelium was seen in two (6.67%) cases while parakeratinization was seen in 28 (93.33%) cases. Stratum granulosum was present in 23.33% of cases in this study. It is not an uncommon finding to notice the stratum granulosum in keratinized epithelia since the keratohyalin granules play an important role in the process of keratinization. In this study, all the lesions (100%) showed the presence of "saw toothed" rete pegs. However, civatte body was observed only in one case. All the 30 biopsies, i.e. 100% of cases, showed the degeneration of basal cell layer of epithelium and the presence of subepithelial cellular infiltrate which varied from mild-to-moderate to severe densities. Also in four biopsies, the ulceration of epithelium leading to disruption of epithelium from the underlying connective tissue was observed.

Table 1: Mean value for response of the subjects for change in parameters at different periods of observation

Group	Surface texture	Color	Burning sensation
A			
Preoperative	1.00	2.80	2.93
At 6 weeks	0.13	2.07	2.00
At 12 weeks	0.20	1.13	1.80
At 24 weeks	0.27	1.20	1.73
B			
Preoperative	1.00	2.80	2.93
At 6 weeks	0.13	2.07	2.00
At 12 weeks	0.20	1.13	1.80
At 24 weeks	0.27	1.20	1.73

Table 2: Mean reduction in the parameters over a period of 24 weeks of observation

	Surface texture	Color	Burning sensation
Group A	0.20	1.47	1.84
Group B	0.20	1.47	1.84

DISCUSSION

Lichen planus is of particular interest to the dentist because involvement of the oral mucous membrane frequently accompanies or precedes the lesions on the skin. It is reported to undergo malignant transformations,[7,49,50] which mandates its definite diagnosis and proper treatment. Available treatments of OLP are not curative, and many have potentially prominent side effects. The objectives of OLP management should be to prevent and screen for malignant transformation and alleviate symptoms on the long term. Avoidance of potential precipitating drugs, tobacco, alcohol, and local trauma, as well as strict oral hygiene, is essential. The first-line pharmacologic treatment relies on topical steroids. Systemic steroids should be limited to the short-term cure of severe refractory OLP. Life-long clinical follow-up, at least annually, is fundamental.[13]

Various treatment modalities have been tried from time to time such as use of corticosteroids,[41,42,51] tranquilizers,[11] griseofulvin,[39,40] etretinate,[23] labial veneers,[52] cyclosporine,[41] iontophoresis,[53] cryosurgery,[22,43] electrosurgery,[44] laser,[46] etc. with varying results. The topical, systemic, and iontophoretic application of the corticosteroids had generally produced good results in patients with

Table 3: Mean reduction and '*t*' value for change in parameters at different periods of observation

Group		Surface texture		Color		Burning sensation	
		Mean reduction	'*t*' value	Mean reduction	'*t*' value	Mean reduction	'*t*' value
A	At 6 weeks	0.87	9.539*	0.73	6.205*	0.93	7.897*
	At 12 weeks	0.80	7.483*	1.67	13.229*	2.93-1.80	6.859*
	At 24 weeks	0.73	6.205*	1.60	9.798*	2.93-1.73	6.874*
B	At 6 weeks	0.87	9.539*	0.73	6.205*	0.93	7.897*
	At 12 weeks	0.80	7.483*	1.67	13.229*	2.93-1.80	6.859*
	At 24 weeks	0.73	6.205*	1.60	9.798*	2.93-1.73	6.874*

*The values are statistically significant at 1% probability level

OLP. Although many surgical treatments such as electrosurgery,[44] cryosurgery,[22,43] and laser surgery[46] had been tried, but recurrence of some of treated areas had been reported.[54]

The ultrastructural sequence of events occurring in lesion formation has been studied by Barnett.[55] These mechanisms may combine to cause T-cell accumulation in the superficial lamina propria, basement membrane disruption, intraepithelial T-cell migration and keratinocyte apoptosis in OLP.[56] Free soft-tissue grafts have also been used for localized areas of erosive OLP.[38] Surgically removed lesions of OLP may recur, but not invariably.[14]

Tamizi and Moayedi[45] reported a case of treatment of gingival lichen planus in which they utilized recipient site prepared for free gingival graft in which periosteum was freed of all submucosal tissue and observed complete disappearance of lesions after 3.5 years. They explained the basis for surgical treatment of lichen planus on the concept that these lesions were caused by lymphocytic aggression toward keratinocytes and suggested such treatment where the complaint could not be resolved with other methods.

Based on the similar rationale, in the present investigation, a surgical procedure comprising of excisional biopsy combined with a bioresorbable membrane placement has been attempted to treat erosive lichen planus of gingiva. A bioresorbable (Polyglactin 910) membrane has been used to provide support to healing wound, stabilize the clot, and enhance regeneration, act as scaffold for healing tissue, alone with acting as a barrier from the underlying submucosal connective tissue.[57] New epithelium has been guided to regenerate in an environment free of any influence from the underlying connective tissue. This study was carried out to evaluate the efficacy of bioresorbable (Polyglactin 910) membrane in the management of erosive lichen planus of gingiva and was compared with the excisional biopsy procedure alone.

The findings of this study in the experimental group (group A) showed a marked improvement in almost 100% of the treated patients. Patients remarked a significant improvement in the color, and surface texture of the gingiva due to meticulous home care measures, plaque control, diet restrictions, proper medications, decreased ulceration, increased keratinization/epithelization, decreased psychological stress due to removal of the lesion, excision of the lesion and placement of bioresorbable membrane, which might have elicited the healing process. The findings of the study indicated that the lesions of erosive lichen planus of gingiva improved substantially with both the techniques employed. However, when group A and group B were compared, the differences in improvement were not statistically significant, showing thereby that the excisional biopsy procedure resulted in equivalent improvement of erosive lichen planus of gingiva. However, no worsening of scores from the baseline was observed for color change, surface texture, and burning sensation of gingiva at the end of the study. Here, it is worth mentioning that statistical significance testing does not necessarily reflect the magnitude of the effect, and if the differences between different study groups are not statistically significant, it does not denote that the differences are not clinically meaningful with regard to a desired outcome. Clinical trials are conducted to answer clinical questions, and clinical parameters are used to monitor outcomes; therefore, the results should refer to the importance of the clinical data before making therapeutic decisions. However, there is no precise way to define clinical relevance regarding how small an improvement is meaningful in every situation.[58]

Clinically, one striking finding during the study was that for all the characteristics included in the study, i.e. surface texture, color, and burning sensation, few patients showed recurrence, after being subjected to both the treatment modalities during the course of the study. For surface texture, in both groups A and B, one patient reported recurrence after 12 weeks of observation, two patients at 24 weeks of observations, and two patients did not improve at all after 6, 12, and 24 weeks of observation. This may be attributed to the ulceration in the epithelium which can be the result of lack in plaque control instructions,[3,59] improper and aggressive tooth brushing,[3,60] allergy,[60] trauma,[3,60] infection (viral,[23,25,60] bacterial,[3,27,60] and fungal[28,29,60]), and psychological stress.[3,23,24,60] The patients who did not improve at all gave a history of being under a constant stress.

No research is quite complete. It is the glory of a good bit of work that opens the way for something still better and rapidly leads to its own eclipse, the objective of research is the advancement, not for the investigator, but of knowledge. Hence, this study although not reaching specific and definitive results

about the clear-cut advantages of one method over the other, it definitely calls on for future studies with longer periods of follow-up, keeping in view the prevention of recurrence of these lesions, as a primary outcome and to analyse the utility of the treatment method for specific variants of OLP.

CONCLUSION

In conclusion, there was a significant improvement of lesion by both the excisional biopsy procedure and excisional biopsy combined with the bioresorbable membrane with statistically nonsignificant difference in the improvement of lesion between two procedures. Worsening of baseline scores was not observed in any case at the end of the study. Although this study does not show any specific and definitive results, it will definitely show some guidelines for future studies.

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