

Comparative Evaluation of Intralesional Injection of Autologous Platelet Rich Plasma Versus Intralesional Injection of Corticosteroids in The Management of Resistant Oral Lichen Planus

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ABSTRACT

Background: Lichen Planus (LP) is a chronic mucocutaneous inflammatory disease that predominantly affects the oral mucosa, with a female predilection. The oral lesions are characterized by burning and pain which relentlessly affect the patient's quality of life. The available treatment approaches for OLP documented to have a short term effect with potential adverse effects which further increases the demand of a novel therapeutic approach for the severe resistant lesions of OLP with a malignant potential. This double-blind, split-mouth randomized controlled trial aims to evaluate and compare the effectiveness of intralesional Autologous Platelet Rich Plasma and corticosteroid for the management of resistant OLP.

Materials and methods: 28 clinically and histopathologically confirmed cases of resistant OLP were included with total 56 lesion sites divided into two groups of 28 each, in group 1 intralesional PRP and in group 2 intralesional steroid was given. The injections were repeated for consecutive 4 weeks and then kept on regular followup. Parameters recorded on every visit were according to the Modified Escudier Index.

Results: A statistically significant reduction in the lesion activity scores was found amongst the group treated with Platelet Rich Plasma as compared to the group treated with intralesional steroids.

Conclusion: The use of intralesional PRP in resistant cases of OLP showed superior results in improving clinical signs to that of intralesional Steroids, without any adverse effects.

Keywords: OLP, Platelet Rich Plasma, Intralesional Steroid

INTRODUCTION

Lichen planus (LP) is a chronic mucocutaneous inflammatory disease that frequently affects the oral mucosa, with predominance towards the middle aged female patients mostly. OLP is estimated to affect 0.5% to 2% of the general population and it tends to be more persistent and more resistant to treatment than the cutaneous

form.¹

OLP can present clinically in six different patterns: papular, reticular, plaque, atrophic, erosive and bullous, each having specific characteristics and can be found isolated or associated together. The most prevalent type of OLP is the reticular type, characterized by the presence of Wickham striae, which are typically symmetric, bilateral and mainly found on the buccal mucosa. The erosive form,

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regardless of being less frequent, has an extra medical importance because the lesions are typically symptomatic and patients usually present slight discomfort to episodes of excessive pain.²

In the pathogenesis of OLP disease, antigen-specific or non-specific mechanisms or both may be involved. Antigen specific mechanisms include antigen presentation by basal keratinocytes and antigen specific keratinocyte killing by CD8+ T-cells. Nonspecific mechanisms include mast cell degranulation and MMPs activation in the lesions. These mechanisms may act simultaneously to cause T-cell accumulation in the superficial lamina propria, basement membrane disruption, T-cell migration, and keratinocyte apoptosis. It has been hypothesized that the chronicity of OLP may be attributed to the TGF- β 1-mediated immunosuppression.³

Topical corticosteroids with their anti-inflammatory and anti-immunologic properties are considered as the first-line pharmacological agents for OLP.⁴ For the erosive type of LP intralesional CS are considered superior to that of topical and systemic as the high concentration of the drug can be achieved with intralesional injections with negligible systemic absorption. Yet various systemic adverse effects have been highlighted in the literature. The complications due to the long term use of corticosteroids include Hypothalamus pituitary adrenal suppression, endocrinal changes as moon face, hirsutism, striae, fungal infections as well as growth retardation. Moreover, local adverse effects including tissue atrophy, candidiasis, granuloma formation and gingival neo-vascularization also have been reported with the use of ILS.^{5,6}

Hence, in light of all the above mentioned adverse effects of CS there is necessity for an alternate treatment with lesser side effects. Platelet Rich Plasma (PRP) is a plasma concentrate of the patient's blood that predominantly contains platelets. Along with the high concentration of platelets, PRP has a very high concentration of coagulation factors. Activated platelets release different growth factors that contribute to cell migration, proliferation, differentiation, angiogenesis, removal of tissue debris and regeneration of the appropriate type of tissues.⁷ PRP helps to accelerate wound healing and improve the patient's quality of life with its anti-inflammatory, anti-oxidative and immunomodulatory action.⁸ Therefore, PRP can be a better novel substitute to the CS without any adverse effects.

To the extent of our knowledge no study has compared the therapeutic effect of intralesional steroids and PRP for the patients of OLP in a split-mouth study design.

Material and Methods

The study was double-blind split-mouth randomized controlled trial which included twenty-five patients, clinically and histopathologically diagnosed with Oral Lichen Planus according to the WHO modified diagnostic criteria (2003)⁹ who reported to the department of Oral Medicine at I.T.S CDSR Ghaziabad. The ethical clearance was provided by the I.T.S institutional ethics committee (IIEC) with protocol number ITSCDSR/IIEC/2019-2022/OMR/01.

All the patients were given a detailed explanation of the study and a signed consent was taken.

A minimum sample size of 20 for each group was calculated using OpenEpi, version 3, open source calculator and software. In our study 28 patients with a total of 56 lesion sites (right and left buccal mucosa) were included and divided into two groups, in group 1- intralesional PRP and in group 2- intralesional steroid (inj. Kenacort 40mg). The injected side for PRP was determined using coin toss method by the physician who injected and a blinded physician scored the severity, the lesion size and take the pain/burning score. The patients were also blind to the nature of injection in each side of buccal mucosa.

Inclusion and exclusion criteria- Patients presenting with a clinical picture that favors the diagnosis of oral lichen planus and histological findings confirming the diagnosis and those who received topical or systemic treatment for OLP in the last 2-4 weeks were included. Patients with Systemic disorder, severe cardiovascular diseases, history of drugs that could cause Lichenoid reaction, any dysplastic lesion, platelet count of < 150,000/mm³ and Hb < 11 g/dl were excluded. Additionally pregnant or breastfeeding females, and the patients who were on anticoagulant therapy and/or used non-steroidal anti-inflammatory drugs in the last 5 days before taking the blood sample were also excluded.

the Modified Escudier Index¹⁰ was used for lesion analysis which include the Site score- 0- absence of the lesion and 1- for the presence of lesion; the Severity score, where 0 means whitish plaque only, 1-keratosis/plaque with mild erythema, 2-marked erythema and 3- presence of ulceration; pain/burning sensation perceived by the patient (recorded using the Visual analog scale of 0-10) where 0 denotes no pain/burning and 10 denotes severe pain/burning.

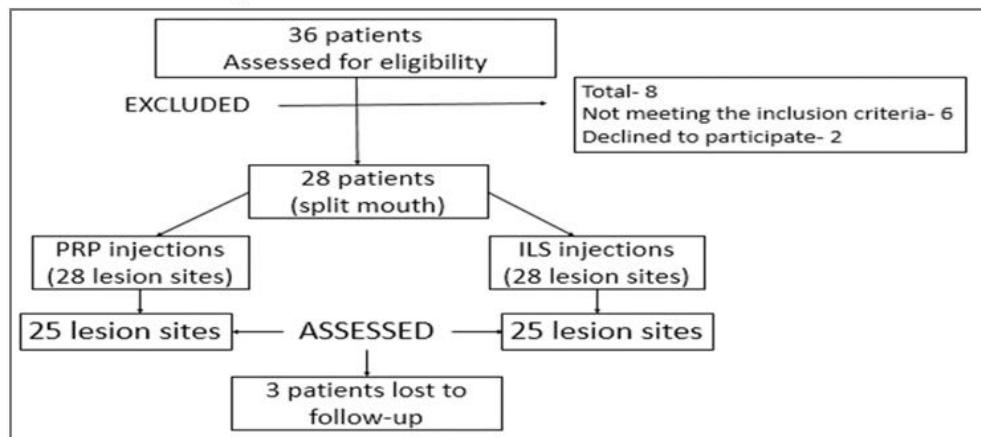
Later the activity score was calculated by multiplying the site and severity score.

For the preparation of PRP, on every visit 10ml of patient's intravenous blood was withdrawn and collected in an anticoagulant tube with the help of oral pathologist. The collected blood was then centrifuged with the regular first spin of 15 minutes which yields PPP (platelet poor plasma) and PRP (platelet rich plasma) then the PRP was transferred to another tube which undergoes a second spin of 10 minutes providing an injectable form of PRP at the bottom of tube with acellular plasma and PPP at the top. With the help of a syringe, the majority of the PPP was removed and disposed, and the rest was injected after shaking thoroughly.

A 25 gauge needle was used for the injections after topically anaesthetizing the buccal mucosa. The steroid and PRP both were injected in a volume 0.5ml per 1cm² of involved mucosa respectively on the same visit. The injections for each group were followed for every 7th day, consecutively for 4 weeks and then patients were kept on a followup for 2 months.

Results-

A total of 36 patients were assessed for eligibility out of which 8 were excluded. 28 patients were included and with the split mouth study design they were divided into 2 groups of 28 lesion sites each with a total of 56 lesions sites from right and left buccal mucosa. 3 patients were lost to follow-up before the end of the trial.



The data obtained at the end of the trial of total 25 patients was analyzed using Statistical Package for Windows; SPSS [ver 22, Armonk, IBM Corp, USA]. Various test applied include The Shapiro-Wilk, Mann Whitney U, Friedman's and Wilcoxon rank test.

Table 1 and table 2 depicts Mean and percentage difference of pain scores and the activity scores at different time intervals by study participants treated with Platelet Rich Plasma and intra lesional steroid.

Table 1: Mean and percentage difference of pain scores at different time intervals by study participants treated with PRP and intra lesional steroid

	Platelet Rich Plasma ^a				Intra-lesional Steroid ^a			
	Mean scores	MD	P value	% difference	Mean scores	MD	P value	% difference
1st visit	9.48 ± 1.0	1.64	P = 0.001*	20.3	9.52 ± 0.82	1.32	P = 0.001*	13.86
2nd visit	7.84 ± 1.45				8.2 ± 0.81			
2nd visit	7.84 ± 1.45	2.36	P = 0.001*	30.1	8.2 ± 0.81	1.76	P = 0.001*	21.46
3rd visit	5.48 ± 1.5				6.44 ± 1.08			
3rd visit	5.48 ± 1.5	1.96	P = 0.001*	35.7	6.44 ± 1.08	1.96	P = 0.001*	30.4
4th visit	3.52 ± 1.55				4.48 ± 0.82			
4th visit	3.52 ± 1.55	1.64	P = 0.001*	46.6	4.48 ± 0.82	1.6	P = 0.001*	35.7
5th visit	1.88 ± 1.13				2.88 ± 0.88			
5th visit	1.88 ± 1.13	0.96	P = 0.01*	51.06	2.88 ± 0.88	1.08	P = 0.05*	37.5
6th visit	0.92 ± 0.49				1.8 ± 0.5			
6th visit	0.92 ± 0.49	0.25	P = 0.01*	26.08	1.8 ± 0.5	0.08	P = 0.65	4.4
7th visit	0.68 ± 0.9				1.72 ± 0.84			

MD-Mean Difference; %-percentage; a-Intra group comparison are significant using Friedman test $P \leq 0.05$ level of significance at $P \leq 0.05$; *statistically significant using Wilcoxon rank sum test

Table 2: Mean and percentage difference in activity score at different time intervals by patients treated by PRP and Intra-lesional Steroid

	Platelet Rich Plasma ^a				Intra-lesional Steroid ^a			
	Mean scores	MD	<i>P</i> value	% difference	Mean scores	MD	<i>P</i> value	% difference
1st visit	5.16 ± 1.62	0.44	<i>P</i> = 0.08	8.52	5.24 ± 1.5	1.32	<i>P</i> = 0.03*	13.86
2nd visit	4.72 ± 1.86				4.52 ± 1.8			
2nd visit	4.72 ± 1.86	2.2	<i>P</i> = 0.001*	46.6	4.52 ± 1.8	1.76	<i>P</i> = 0.001*	21.46
3rd visit	2.52 ± 1.68				3.16 ± 1.8			
3rd visit	2.52 ± 1.68	1.36	<i>P</i> = 0.001*	53.9	3.16 ± 1.8	1.96	<i>P</i> = 0.001*	30.4
4th visit	1.16 ± 1.02				2.2 ± 1.63			
4th visit	1.16 ± 1.02	0.48	<i>P</i> = 0.11	41.3	2.2 ± 1.63	1.6	<i>P</i> = 0.001*	35.7
5th visit	0.68 ± 0.47				0.68 ± 0.74			
5th visit	0.68 ± 0.47	0.68	<i>P</i> = 0.001*	68	0.68 ± 0.74	0.64	<i>P</i> = 0.003*	62.1
6th visit	0				0.04 ± 0.2			
6th visit	0	0	-	-	0.04 ± 0.2	-0.08	<i>P</i> = 0.98	-20
7th visit					0.12 ± 0.3			

MD-Mean Difference; %-percentage; a-Intra group comparison are significant using Friedman test $P \leq 0.05$ level of significance at $P \leq 0.05$;

*statistically significant using Wilcoxon rank sum test
Statistically no significant difference was found in the distribution of activity scores between 1st to 2nd visit and between 4th to 5th visit in the group treated with Platelet Rich Plasma. But there was a significant difference

Figure 1 and 2- showing Group-1 treated with Intralesional PRP



Fig. 1- Baseline/ Pre-Treatment



Fig. 2- After 4 therapies by intralesional PRP

Figure 3 and 4- showing Group- 2 treated with Intralesional triamcinolone acetonide

between activity scores at every visit in the group treated with Intra lesional steroid except between 6th and 7th visit ($P = 0.98$).

On comparison of activity scores at different follow up between two groups a statistically significant reduction was observed on 4th , 6th and 7th visit among the group treated with Platelet Rich Plasma along with a significant reduction in pain scores at 3rd, 4th, 5th ,6th and 7th visit respectively.



Fig. 3- Baseline/ Pre-Treatment



Fig. 4- After 4 therapies by Intralesional Steroids

Discussion

LP is a defect of the stratified squamous epithelia which affects a large number of population.¹¹ The lesions of LP involving the skin generally improve within a duration of two years, but in OLP it could last up to 20 years or even more.¹² The oral mucosa is a common site of involvement, and it may be the only representing site in 0.5 to 2% of the population.

OLP is a chronic disorder with predictable flare-ups and symptom-free periods where each patient's disease behavior can differ.¹³ Hence, the goal of different available treatments is to alleviate unpleasant symptoms, curtail ulcerative lesions, extend symptom-free periods, and mitigate the risk of oral cancer. In the mild cases of OLP various topical preparations of steroids can be used but in the cases of erosive OLP systemic steroids are prescribed extensively which has the major limitation of potential adverse effects. Another treatment options are immunosuppressant and immunomodulatory drugs, which can have a major drawback of promoting malignant transformation with prolonged use, theoretically.¹⁴ In comparison to corticosteroids, PRP has a stronger safety profile with little or no side effects.^{15,16} In the present study, patients were recalled every week till the 5th visit for PRP then for monthly follow-up for next 2 months.

The activity scores were found to be significantly reduced in the group treated with PRP as compared to the one treated with intralesional steroid which is in contrary to the results of the studies conducted by Ahuja US et al. where they compare the efficacy of ILS and PRP for the management of erosive LP and reported a comparative efficacy of both intralesional steroids and PRP for the treatment/management of OLP.¹⁷ This variation could be due to the larger sample size of our study.

Merigo et al. in their case report used platelet rich plasma rinses for the patient with non-responding erosive lichen planus after trying all other modalities including the topical and systemic steroids, low-level laser therapy etc and advocated the efficiency of PRP over other modalities.¹⁸

Lore et al. compared the effects of PRP gel with cyclosporine mouthwash and retinoic acid lotion in various types of OLP in a pilot study and came to the conclusion that the use of PRP could be effective in the management of erosive form when applied weekly.¹⁹

In our study, none of the patients report any adverse effect during the follow-up period. Five patients report recurrence in the form of slight burning sensation on the side treated with intralesional steroids on the 7th visit.

Conclusion-

The present study promotes the use of intralesional PRP for the management of resistant OLP, as its results are superior to that of intralesional steroids with no side effects. Further research with a larger sample size and longer follow-up is needed to validate the PRP as a standard treatment in OLP.

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Conflict of interest- NIL

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