

Computerised Photometric Analysis of Photodynamic Therapy versus Triamcinolone Acetonide for Treatment of Erosive Lichen Planus- A Prospective Interventional Study

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ABSTRACT

Introduction: Lichen planus is a mucocutaneous disease of unknown aetiology. Topical corticosteroid has been widely used for the treatment purpose so far. In order to overcome the side-effects of corticosteroid, Photodynamic Therapy (PDT) has been proposed, but very few studies have been done to evaluate the effect of PDT and corticosteroid on lichen planus using computerised photometric analysis.

Aim: To compare the efficacy, using computerised photometric analysis and Red Green Blue (RGB) scoring, of triamcinolone acetonide and PDT in the treatment of erosive lichen planus.

Materials and Methods: This prospective interventional study was done in the Department of Oral Medicine and Radiology, Kalinga Institute of Dental Sciences, Bhubaneswar, Odisha, India, from January 2021 to February 2021. There were 10 patients of erosive lichen planus who were divided into two groups. Patients of group A were treated with triamcinolone acetonide, and group B patients were treated with PDT, for four weeks. Visual Analogue Score (VAS), Reticular Erosive Ulcerative (REU) Score, Oral Mucositis Index (OMI), photometric analysis using RGB

scoring were recorded at baseline, after two weeks and four weeks of treatment. Mann-Whitney U test was used for intergroup comparison, and paired t-test for intragroup comparison.

Results: In the study, there was no significant difference (p-value=1.00) in age among the patients of two groups. At baseline, VAS mean score of group A patients (5.20±0.837), group B patients (6.40±1.140) and the p-value was 0.101; REU mean score of group A patients (5.90±1.245), group B patients (9.00±2.00) and p-value was significant (0.028); OMI mean score of group A patients (1.20±0.447), group B patients (1.60±0.548) and p-value was 0.221; RGB mean score for group A (110.80±1.212) and group B (116.52±1.194). After four weeks of treatment, VAS mean score of group A patients was (0.80±0.84), group B patients was 0, with p-value=0.05; REU mean score in group A (2.70±1.04), group B (1.00±0.71), p-value=0.031; OMI mean score of both group A and B was 0; RGB mean score for group A (113.22±1.89), group B (121.58±0.96), p-value=0.009.

Conclusion: It was found that PDT was better in treating erosive lichen planus and it can be used as an alternative to the standard treatment modalities.

Keywords: Corticosteroid, Red green blue analysis, Visual analogue score

INTRODUCTION

Lichen planus is a chronic mucocutaneous disorder which affects the oral mucosa and skin [1]. It occurs more commonly in middle aged women with occurrence rate of 0.5-2.2% [2]. It is a potentially malignant condition with malignant transformation rate of 0.4-5.6% [3]. Oral Lichen Planus (OLP) has six clinical subtypes-reticular, papular, plaque-like, bullous, erosive and ulcerative [1]. Lesions can occur on any mucosa but most commonly occur on buccal mucosa. Papular, reticular, plaque-like, bullous are asymptomatic while erosive and ulcerative subtypes are symptomatic lesions. Symptoms can vary from mild pain to extremely painful lesions which interfere with eating [1].

Aetiology of OLP is unknown. During recent years, it has become more evident that the immune system has a primary role in the development of the disease. Several investigators proposed that psychological factors have a strong association with lichen planus [4,5]. Psychological factors like high stress and anxiety levels are associated with lichen planus [6,7].

At present, topical and systemic corticosteroids are mainly used for treatment of OLP. However, long term use of corticosteroids for chronic OLP has undesired local and systemic complications. In order to overcome the side-effects of corticosteroid, PDT has been proposed as a treatment strategy for OLP. The PDT

is a procedure based on the activation of molecules of various chemical agents called photosensitisers by light emitting radiation using a selected wavelength. After activation, cytotoxic free radicals are released and subsequently result in the destruction of targeted cells [8].

Mattsson U et al., used photometric analysis using RGB scoring for diagnostic purpose of oral lichenoid reaction only [9]. No study is done till date to assess the erosive lichen planus lesions using photometric analysis. So in the present study, RGB was used to compare the efficacy of triamcinolone acetonide and PDT in treatment of erosive lichen planus with the aid of computerised photometric analysis using RGB scoring. The VAS, OMI, REU scoring were used for clinical evaluation of the lesions.

MATERIALS AND METHODS

A prospective interventional study was carried out in the Department of Oral Medicine and Radiology, Kalinga Institute of Dental Sciences, KIIT Deemed to be University, Bhubaneswar, Odisha, India, from January 2021 to February 2021. After Institutional Ethics Committee approval (Letter IEC/168/2020) and obtaining written consent form, 10 erosive lichen planus patients were selected for the study.

Sample size calculation: Comparisons of the mean difference between the different groups were taken into consideration. Two-sided test done with 80% power and 5% level of significance.

Formula of calculating sample size [10]:

$$n = \frac{(r+1)(SD)^2 (Z_{\alpha/2} + Z_{\beta})^2}{d^2}$$

Where, n=sample size required in each group,

r=Correlation coefficient between the groups=0.3604

d=Expected mean difference between the groups=7.3 [10]

SD=Standard Deviation

$Z_{\alpha/2}$: This depends on level of significance, for 5% this is 1.96

Z_{β} : This depends on power, for 80% this is 0.84

Based on above formula the sample size required per group is five.

Hence, total sample size required was 10.

Inclusion criteria: Patients diagnosed with erosive and ulcerative OLP were included.

Exclusion criteria: Patients with papular, reticular, plaque-like, bullous type lichen planus, quid induced lichenoid reactions. Patients diagnosed with diabetes mellitus and immunocompromised conditions (graft versus host disease, systemic lupus erythematosus) were excluded.

The 10 patients of erosive lichen planus were divided into two groups of five patients each. Group A patients were treated with topical triamcinolone acetonide, and group B patients were treated with PDT.

Study Procedure

Case history was recorded, and oral examination for evaluation of presence of erosive, ulcerative areas within the oral cavity of the selected patients were done. Clinical assessment of each patient was done at 1st visit, two weeks and four weeks after initiation of the treatment by estimating the pain using VAS [11], and OMI [12].

For evaluation of the extent of the lesion, Reticular, Erosive, Ulcerative scoring (REU scoring) [13] was done. For REU scoring the oral cavity of each individual was divided into 10 sites. The severity of the lesions in each site was scored according to the presence of reticular/hyperkeratotic, erosive/erythematous, and/or ulcerative lesion(s) as follows: reticular/hyperkeratotic lesions were scored from 0 to 1 (0=no white striations, 1=presence of white striations or keratotic papules); erosive/erythematous areas were scored from 0 to 3 by area of involvement (0=no lesion, 1=lesions less than 1 cm², 2=lesions from 1 to 3 cm², 3=lesions greater than 3 cm²); ulcerative areas were scored from 0 to 3 by area of involvement (0=no lesion, 1=lesions less than 1 cm², 2=lesions from 1 to 3 cm², 3=lesions greater than 3 cm²). For each of the three clinical signs, a score was derived by summation of the scores of all 10 areas: reticular score=ΣR, erythema score=ΣE, and ulcerative score=ΣU (REU score) with a total weighted score of ΣR+Σ (E×1.5)+Σ(U×2.0) [13].

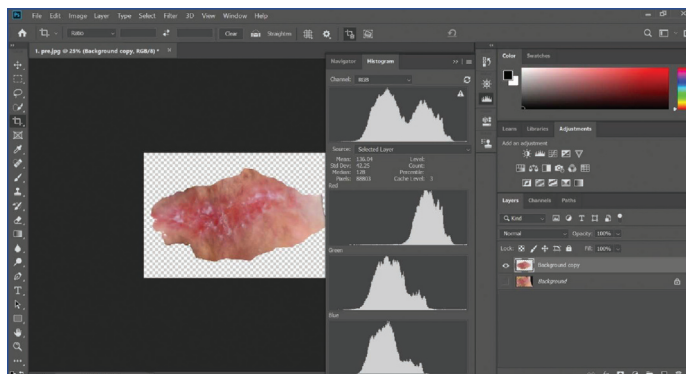
Photometric analysis of lesions were done by RGB scoring [9]. For the photometric analysis, a photograph was taken with the help of Digital Single-lens Reflex (DSLR) camera. The images obtained were transferred to the computer and analysed with the help of Adobe Photoshop CS5. For each image the mean RGB values were recorded and tabulated on each visit [Table/Fig-1-8]. RGB i.e., the primary colours in the additive colour synthesis. A RGB file consists of composite layers of RGB, each being coded on 256 levels from 0 to 255. For example, black corresponds to the levels of R=0, G=0, B=0 and white corresponds to the levels R= 255, G=255, B=255 [9]. RGB scores for a given lesion will increase with the degree of healing of the lesion.

Treatment of the lesion:

- Group A- Patients were advised for topical application of 0.1% triamcinolone acetonide three times daily for one month.
- Group B- PDT was administered on two appointments per week for one month. In each appointment-



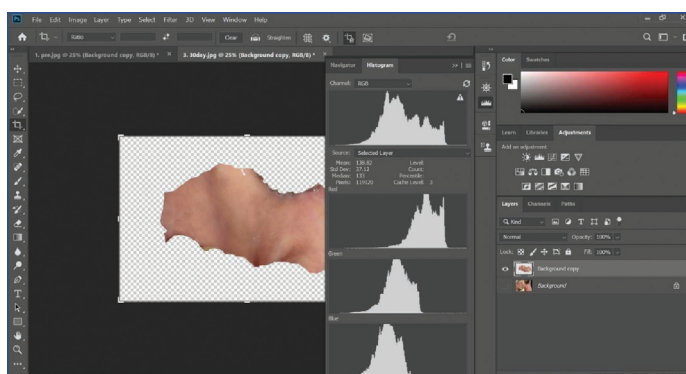
[Table/Fig-1]: Triamcinolone Acetonide treated case picture on first visit.



[Table/Fig-2]: Triamcinolone Acetonide treated case picture- RGB analysis on first visit.



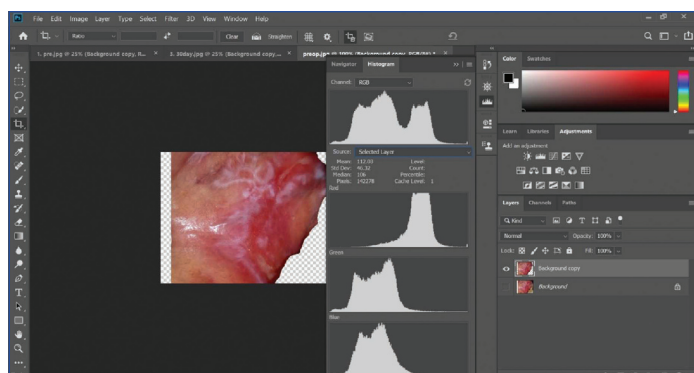
[Table/Fig-3]: Triamcinolone Acetonide treated case picture on follow-up after four weeks of initiation of treatment.



[Table/Fig-4]: Triamcinolone Acetonide treated case picture- RGB analysis after four weeks of initiation of treatment.



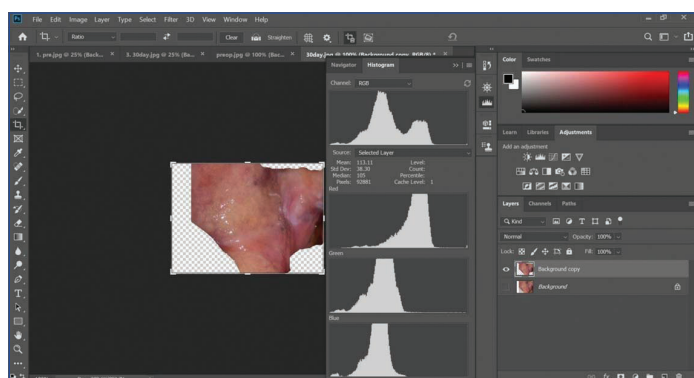
[Table/Fig-5]: Photodynamic Therapy treated case picture on first visit.



[Table/Fig-6]: Photodynamic Therapy treated case picture- RGB analysis on first visit.



[Table/Fig-7]: Photodynamic Therapy treated case picture on follow-up after four weeks of initiation of treatment.



[Table/Fig-8]: Photodynamic Therapy treated case picture- RGB analysis after four weeks of initiation of treatment.

- Topical application of 50 µg toluidine blue (1 mg/mL) with micropipette on the lesions were done. After 10 min it was treated by laser radiation using diode laser (980 nm wavelength, 0.1 Watt, 18 Joule, continuous wave, spot size 1 cm²). Laser irradiation was done in three cycles, each cycle duration was of three minutes [14].

STATISTICAL ANALYSIS

Data obtained was analysed with Statistical Package for the Social Sciences (SPSS) software version 26. Comparison of the scores of the intergroup was done by Mann-Whitney U test and for intragroup comparison paired t-test was used. The p-value was considered significant at less than 0.05.

RESULTS

The demographic data given in [Table/Fig-9] shows that mean age of individuals in group A was 32.60±17.75 and in group B was 47.20±6.68. No significant difference was noted in age between two groups. There was 80% male population and 20% female population in group A whereas 40% males and 60% females were present in group B. The descriptive statistics of the groups at baseline have been mentioned in [Table/Fig-10]. The mean statistics of VAS scores for the photodynamic group was 6.40±1.140 and for

triamcinolone acetate group it was 5.20±0.837. The REU score for the photodynamic group was 9.00±2.00 and triamcinolone acetate group it was 5.90±1.245. The OMI scores for photodynamic group were 1.60±0.548 and for triamcinolone acetate groups it was 1.20±0.447. The RGB values for photodynamic group were 116.52±1.194, and for the triamcinolone acetate groups it was 110.80±1.212. Significantly higher REU and RGB score was noted in the photodynamic group.

Parameters	Group A	Group B	Chi-square/p-value
Age, in years (Mean±SD)	32.60±17.757	47.20±6.686	0.00/1.00
Gender, n (%)	Male	4 (80)	0.400/0.527
	Female	1 (20)	
Total	5 (100)	5 (100)	

[Table/Fig-9]: Demographic data of two groups.

Group	VAS (Mean±SD)	REU (Mean±SD)	OMI (Mean±SD)	RGB (Mean±SD)
Group A	5.20±0.837	5.90±1.245	1.20±0.447	110.80±1.212
Group B	6.40±1.140	9.00±2.000	1.60±0.548	116.52±1.194
Z score	-1.638	-2.200	-1.225	-2.611
p-value	0.101	0.028*	0.221	0.009*

[Table/Fig-10]: Descriptive statistics at baseline. *statistically significant **Mann-Whitney U test was used
VAS: Visual analogue score; REU: Reticular erosive ulcerative score; OMI: Oral mucositis index; RGB: Red green blue; p-value <0.05 considered significant

The descriptive statistics of the groups after two weeks have been mentioned in [Table/Fig-11]. The mean statistics of VAS scores for the photodynamic group was 2.40±0.548 and for triamcinolone acetate group it was 3.00±1.225. The REU score for the photodynamic group was 3.60±1.949 and triamcinolone acetate group it was 3.90±0.962. The OMI scores for photodynamic group were 0.80±0.447 and for triamcinolone acetate group it was 0.60±0.548. The RGB values for photodynamic group were 119.55±0.854, and for the triamcinolone acetate groups it was 111.59±1.779. Significantly higher RGB score was noted in photodynamic group.

Group	VAS (Mean±SD)	REU (Mean±SD)	OMI (Mean±SD)	RGB (Mean±SD)
Group A	3.00±1.225	3.90±0.962	0.60±0.548	111.59±1.779
Group B	2.40±0.548	3.60±1.949	0.80±0.447	119.55±0.854
Z score	-0.808	-0.973	-0.655	-2.611
p-value	0.419	0.331	0.513	0.009*

[Table/Fig-11]: Descriptive statistics for the variables after two weeks. *statistically significant ** Mann-Whitney U test was used; p-value <0.05 considered significant

The descriptive statistics of the groups after four weeks have been mentioned in [Table/Fig-12]. The mean statistics of OMI scores was 0 in both the groups and VAS scores of triamcinolone acetone group was 0.80±0.84. The REU score for the photodynamic group was 1.00±0.71 and triamcinolone acetate group it was 2.70±1.04. The RGB values for photodynamic group were 121.58±0.96, (normal mucosa RGB score ranges from 110-130) and for the triamcinolone acetate groups it was 113.22±1.89. Significantly, higher RGB and lower VAS and REU score was noted in photodynamic group.

Group	VAS	REU	OMI	RGB
Group A	0.80±0.84	2.70±1.04	0	113.22±1.89
Group B	0	1.00±0.71	0	121.58±0.96
Z score	-1.936	-2.162	0	-2.611
p-value	0.05*	0.031*	1.000	0.009*

[Table/Fig-12]: Mann-Whitney U statistics for the variables after four weeks. *statistically significant; **Mann-Whitney U test was used; p-value <0.05 considered significant

Intragroup comparison is given in [Table/Fig-13]. A statistically significant difference was noted for the VAS scores in both the

groups at individual follow-ups. A statistically significant difference was noted for the REU scores in both the groups at individual follow-ups. For the OMI score, there was no statistically significant difference noted for the first week and second week scores for both the groups. There was a statistically significant difference between the first week and fourth week values for both the groups. No statistically significant difference was noted between the first week and second week follow-up for the triamcinolone acetate group while a statistically significant difference was noted in photodynamic group. A statistically significant difference was noted for the RGB scores in both the groups at one week and four week follow-ups.

Variables		Mean±SD	t	p-value	
Group A	VAS	1 week-2 week	2.20±0.837	5.880	0.004*
		1 week-4 week	4.40±1.517	6.487	0.003*
	REU	1 week-2 week	2.00±0.500	8.944	0.001*
		1 week-4 week	3.20±0.570	12.551	<0.0001*
	OMI	1 week-2 week	0.60±0.548	2.449	0.070
		1 week-4 week	1.20±0.447	6.000	0.004*
	RGB	1 week-2 week	-0.79±0.650	-2.717	0.053
		1 week-4 week	-2.422±1.384	-3.911	0.017*
Group B	VAS	1 week-2 week	4.00±0.707	12.649	<0.0001*
		1 week-4 week	6.40±1.14	12.551	<0.0001*
	REU	1 week-2 week	5.40±1.29	9.330	0.001*
		1 week-4 week	8.00±1.65	10.787	<0.0001*
	OMI	1 week-2 week	0.80±0.837	2.138	0.099
		1 week-4 week	1.60±.548	6.532	0.003*
	RGB	1 week-2 week	-3.032±0.602	-11.255	<0.0001*
		1 week-4 week	-5.060±0.587	-19.262	<0.0001*

[Table/Fig -13]: Intragroup comparison of variables at baseline, after 2nd week and four weeks.

*statistically significant; †paired t-test was used; p-value <0.05 considered significant

DISCUSSION

In the present study, 10 erosive lichen planus patients were divided into two groups, group A and group B; patients in group A were treated with topical application of triamcinolone acetonide and the patients in group B were treated with PDT. Scores of the group treated with PDT was significantly less than the group treated with topical triamcinolone acetonide. Photodynamic possess physiological effects include aggregation of prostaglandins, immunoglobulins and lymphocytes as well as beta-endorphin and enkephalin in tissues, resulting in reduction of inflammation, immune response and pain [15].

Sadaksharam J et al., evaluated the effect of methylene blue mediated PDT on OLP in 20 patients [16]. This study, which only examined the severity of lesions, showed a significant reduction in their clinical severity, results of this study is in accordance with results of the present study. Dillenburg CS et al., compared the efficacy of laser phototherapy with topical clobetasol for treatment of OLP [17], results of their study showed laser phototherapy was more effective than topical clobetasol which is similar to the results of the present study.

Ferri EP et al., estimated the efficacy of photobiomodulation to treat OLP [18]. They used VAS score, functional score to evaluate the outcome. Both VAS score, functional score was significantly less in patients treated with photobiomodulation than clobetasol propionate. In the present study, PDT was used in place of photobiomodulation therapy but the results were similar. Aghahosseini F et al., studied the effect of methylene-blue mediated PDT on OLP [19]. Improvement in signs of the lesions were noted which is similar to the results of the present study.

Albanese G et al., evaluated the efficacy of low-level laser irradiation on OLP [20], results of their study showed reduction in VAS score and size of lesion which is in accordance to the results of the present

study. Trehan M and Taylor CR, in their study they used low-level 380 nm excimer laser radiation for treatment of OLP [21], VAS score reduced to great extent at the end of the study, results are similar to the present study although different wavelength laser was used.

Jajarm HH et al., compared the effect of low intensity laser therapy with topical corticosteroids in the treatment of erosive and atrophic lichen planus [22]. No significant difference in results was noted between the two treatment modalities whereas in the present study significantly lower scores of pain were noted in patients treated with PDT. Shenawy HM El et al., conducted a study was to evaluate the effect of low level laser therapy versus topical steroids for treatment of erosive-atrophic planus [23]. The VAS score were less in patients treated with topical steroids than low-level laser therapy. Results of this study are in contrary to results of present study.

Othman NA et al., evaluated the effect of laser and topical steroid for treating symptomatic OLP and evaluation was done using VAS score, Tumour Necrosis Factor alpha (TNF alpha) score before and after treatment [24]. Topical steroids reduced both VAS score, TNF-alpha score more than laser therapy. Results of this study are in contrary to results of present study.

In the present study, mean RGB score was recorded for each lesion on first appointment, after two weeks and four weeks, the mean RGB score increased with healing of the lesion in both the groups, but significant increase in mean RGB score was noted in patients treated with PDT than topical steroid application.

Limitation(s)

Long term review of the patients should be done to assess the efficacy of PDT in prevention of recurrence of the lesions.

CONCLUSION(S)

The present study shows that VAS, REU, OMI score was lower and RGB score was higher in patients treated with PDT than individuals treated with triamcinolone acetonide. The PDT is better in treating erosive lichen planus and it can be used as an alternative to the standard treatment modalities. Long term use of corticosteroids can be avoided in chronic cases of OLP. However, in order to evaluate the efficacy of PDT further, randomised control trial with large sample size and long follow-up is needed.

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