Original Article

Treatment of Symptomatic Oral Lichen Planus

Efficacy of Pimecrolimus Cream and Triamcinolone Acetonide Paste in the Treatment of Symptomatic Oral Lichen Planus

Hafiz Muhammad Aamir Riaz, Ayesha Shakeel, Maryam Ali Shaheen and Khurram Jaa

ABSTRACT

Objective: To compare the efficacy of pimecrolimus cream and triamcinolone acetone paste in the treatment of symptomatic oral lichen planus.

Study design: Randomized control trail.

Place and Duration of study: This study was conducted at the Dental Section, Allied Hospital, Faisalabad, from 3rd June 2016 to 31 December 2016.

Materials and Methods: Total no. of 36 patients was included in this study. Consecutive non probability sampling technique was used to calculate the sample size from the reference study by Farzam Gorouhi et al. Ethical approval was obtained from hospital ethical committee and informed consent was taken from the patients before the start of the study. Thirty six patients were randomly divided into two equal groups, eighteen patients in each group Primary outcome was measured by the difference of severity of pain by visual analogue scale at two months from baseline. Oral Health Impact Profile, clinical score and occurrence of side effects were the secondary outcomes measured at each treatment and follow up visit. Computer software SPSS version 23 was used to analyze the data. Data obtained at the end of the treatment in the form of visual analogue scale score, oral health impact profile scores and clinical scores, was compared with baseline scores. Chi square and T test was applied to find out the associated significance variables among the groups.

Results: Overall, there were 100% (n=36) patients; the study population was subdivided into two groups; group A (Pimecrolimus) and group B (Triamcinolone). The mean age, disease duration, VAS pain score, OHIP score and clinical score of the patients in group A was 44.50±6.20 years, 10.61±6.26 days, 5.72±2.32, 3.27±1.17 and 2.38±1.03 respectively, while the mean age, disease duration, VAS pain score, OHIP score and clinical score of the patients in group B was 45.72±5.35 years, 16.77±5.49 days, 6.77±1.43, 3.5±1.42 and 2.83±1.15 respectively. The mean VAS pain score after 1, 2 and 4 months, in group A, was 5.33±1.37, 3.83±1.29 and 3.22±1.39 respectively, while the mean VAS pain score after 1, 2 and 4 months, in group B, was 6.72±1.32, 5.33±1.28 and 4.0±1.57 respectively. The mean OHIP score after 1, 2 and 4 months, in group A, was 1.20±0.90, 2.10±1.42 and 1.45±1.03 respectively, while the mean OHIP score after 1, 2 and 4 months, in group B, was 1.26±1.04, 2.41±1.23 and 1.45±1.08 respectively. The mean clinical score after 1, 2 and 4 months, in group A, was 0.31±0.18, 0.95±0.36 and 0.58±0.44 respectively while the mean clinical score after 1, 2 and 4 months in group B was 0.31±0.16, 0.79±0.23 and 0.51±0.53 respectively. There was significant difference between groups on the basis of VAS score, OHIP score and Clinical score.

Conclusion: According to our study there is significant difference between the efficacy of pimecrolimus cream and triamcinolone acetonide paste, when used for treatment of symptomatic OLP with pimecrolimus cream scoring better than triamcinolone acetonide paste.

Key Words: Lichen planus, Pimecrolimus, Triamcinolone acetonide

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INTRODUCTION

Chronic inflammatory dermatitis of skin and mucous membrane is known as lichen planus[1].

Dental Section, Allied Hospital, Faisalabad.

Correspondence: Dr. Hafiz Muhammad Aamir Riaz, Dental Section, Ex-House Officer, Allied Hospital, Faisalabad.
Contact No: 0300-9644262
Email: h.amirriaz12@gmail.com

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Lichen planus was named so by Erasmus Wilson in 1869, and he also delineated it. Lichen planus is a derivation from Greek word "Lichen" and Latin word "Planus" (Lichen means tree moss and planus means flat)[2]. Incidence of this disease in different populations ranges from 0.1% to 4%. Age group of 30-60 years is affected the most and it is more commonly found in women while very rare incidence in children[3]. Clinical presentation of lichen planus is as papules, plaques, erosions, striations, erythema or blisters, and most affected parts are tongue, buccal mucosa and gingival

part etc[4]. Urgent treatment is required for most symptomatic form like erosive, bullous and atrophic form but the reticular form is most common and is usually asymptomatic.

Various systemic and topical treatment options have been in practice, including which are topical and systemic immunosuppressants like, griseofulvin, corticosteroids, hydroxychloroquine, dapsone, tarcolimus, dapsone, etc[5]. Up till now not a single one of these treatments have been proved to be fully effective and resolutive, which makes the management of symptomatic oral lichen planus a baffling therapeutic challenge. Multiple wide spectrum topical and systemic treatments are in use for management of oral lichen planus but most of these therapies haven't been used in randomized control trails. In management of oral lichen planus corticosteroids have been proved to be very beneficial because of their anti-inflammatory and anti-immunological characteristics by suppressing T cell activity, but their extensive use can prove harmful because of corticosteroids related adverse effects[6]. Pimecrolimus cream 1% is tolerable and quite effective in adult patients of atopic type of oral lichen planus and it is a selective calcineurin inhibitor[7]. The aim of this particular study is to compare clinical safety and efficacy of topical pimecrolimus 1% and triamcinolone acetonide 0.1% paste which is more commonly used to treat oral lichen planus.

Although many treatment options are available and are in common use, despite of these therapeutic modalities, there is no definite treatment of this oral lesion and there are many treatment failures[8]. Corticosteroids are treatment of choice for oral lichen planus and triamcinolone acetonide paste is most commonly used commercial preparation; but because of adverse effects of corticosteroids in some patients, supplementary treatments are applied as necessary option for patients of oral lichen planus.

A novel drug, nonsteroidal topical immunomodulator known as pimecrolimus has been found to be extensively used in treating inflammatory skin and mucosal conditions and also for treatment of oral lichen planus, with efficient results[9]. Pimecrolimus acts by binding to macrophillin 12 and thus prevents dephosphorylation of activated T-cells by calcineurin[10]. This leads to marked reduction of TH1 cytokines production and inhibition of mast cell production of pro-inflammatory cytokines. The main attribute of this treatment is that it inhibits the T-cell mediated pathogenesis of oral lichen planus.

Previously there is lack of randomized control trails in which efficacy of these two drugs have been compared. This study is focused on comparing the relative efficacy of pimecrolimus 1% cream and triamcinolone acetonide 0.1% paste. So that better recommendations can be made for the treatment of lichen planus. Reference study for current article is a study by Farzam Gorouhi et al[11].

MATERIALS AND METHODS

The study was conducted in Dental Section, Allied Hospital, Faisalabad, from 3rd June 2016 to 31 December 2016. Total no. of 36 patients was included in this study. Study design is randomized control trail. Consecutive non probability sampling technique was used to calculate the sample size from the reference study by Farzam Gorouhi et al [11]. Thirty six patients were divided into two equal groups. Patients older than 8 years and clinically diagnosed as oral lichen planus were included in this study. Exclusion criteria was set as; malignancy or viral infection in mouth, patients receiving topical treatment for oral lichen planus in last two weeks or systemic treatment in last four weeks, patients using cyclosporine, psoralen, azathioprine plus ultraviolet A or B in last month, or patients with history of to the drugs under study. Ethical approval was obtained from hospital ethical committee and informed consent was taken from the patients before the start of the study.

Thirty six patients were randomly divided into two equal groups, eighteen patients in each group. Patients in group A were asked to apply pimecrolimus 1% cream four times a day, for two months, and were instructed to avoid smoking, drinking and eating for 20 minutes after applying the cream. Chlorhexidine mouth wash was recommended to be used every night before sleeping. In group B triamcinolone acetonide paste was applied as 1% three times a day at bedtime and after meals on the lesions. Assessment was carried out on monthly basis during the treatment i.e. two months, with a visit each month (three visits in total) and a final follow up assessment was done after two months of completion of treatment (fourth visit). All the visits were attended and assessed by the person conducting this research. Diagnosis was based upon the identification of a marker lesion, which was assessed for reticulation, ulceration, and erosion by visual clinical examination, by clinical scoring in which 0 represented no lesion, 1 for mild white striae, 2 for white striae with atrophic area less than 1 cm, 3 for white striae with atrophic area more than 1 cm, 4 for white striae with erosive area less than 1 cm and 5 for white striae with erosive area more than 1 cm.

Visual analogue scale (100mm) was used by the patients to grade the severity of pain and burning sensation. Oral Health Impact Profile was used to measure the quality of life which consisted of fourteen item questionnaire. Oral Health Impact Profile measures patient's perception of impact of oral conditions on their health. In each treatment visit and follow up visit, patients were examined for vital signs, assessed for side effects if there were any and condition of oral mucosa was examined for any atrophy,

dermatitis, dysplasia, telangiectasia or viral/fungal infection. Primary outcome was measured by the difference of severity of pain by visual analogue scale at two months from baseline. Oral Health Impact Profile, clinical score and occurrence of side effects were the secondary outcomes measured at each treatment and follow up visit. Computer software SPSS version 23 was used to analyze the data. Data obtained at the end of the treatment in the form of visual analogue scale score, oral health impact profile scores and clinical scores, was compared with baseline scores. Chi square and T test was applied to find out the associated significance variables among the groups.

RESULTS

Overall, there were 100% (n=36) patients; the study population was subdivided into two groups; group A (Pimecrolimus) and group B (Triamcinolone). The mean age, disease duration, VAS pain score, OHIP score and clinical score of the patients in group A was 44.50±6.20 years, 10.61±6.26 days, 5.72±2.32, 3.27±1.17 and 2.38±1.03 respectively, while the mean age, disease duration, VAS pain score, OHIP score and clinical score of the patients in group B was 45.72±5.35 years, 16.77±5.49 days, 6.77±1.43, 3.5±1.42 and 2.83±1.15 respectively. There were 11.1% (n=2) males and 88.9% (n=16) females, in group A, and 33.3% (n=6) males and 66.7% (n=12) females, in group B. Morphologic subtype (Erosive/Cerative) noted as 61.1%, Erythemaous/atrophic 16.7% and Morphologic subtype (Reticular) noted as 27.8%, in group A. While, in group B, Morphologic subtype (Erosive/Cerative) noted as 72.2%, Erythemaous/atrophic 5.6% and Morphologic subtype (Reticular) noted as 33.3%. The baseline characteristic of the 36 patients is shown in table 1. Upon statistical analysis, no significant statistical differences were found between under study treatment groups, in regard to disease characteristics before the start of the treatment and demographics, except disease interval (p=0.004).

Summary of intention to treat result and per protocol for VAS score, OHIP score and clinical score has been demonstrated at the interval of 1 month, 2 months and 4 months in each group respectively in table no. 2. The mean VAS pain score after 1, 2 and 4 months, in group A, was 5.33±1.37, 3.83±1.29 and 3.22±1.39 respectively, while the mean VAS pain score after 1, 2 and 4 months, in group B, was 6.72±1.32, 5.33±1.28 and 4.0±1.57 respectively. The mean OHIP score after 1, 2 and 4 months, in group A, was 1.20±0.90, 2.10±1.42 and 1.45±1.03 respectively, while the mean OHIP score after 1, 2 and 4 months, in group B, was 1.26±1.04, 2.41±1.23 and 1.45±1.08 respectively. The mean clinical score after 1, 2 and 4 months, in group A, was 0.31±0.18, 0.95±0.36 and 0.58±0.44 respectively while the mean clinical score after 1, 2 and 4 months in group B was 0.31±0.16, 0.79±0.23 and 0.51±0.53 respectively. There was significant difference between groups on the basis of VAS score, OHIP score and Clinical score. Reason for similar results in regarding per protocol and intention to treat analysis was that all the patients attended their 2nd visit at the end of the 1st month.

Table No.1: Baseline characteristics of study population in two treatment groups

Variable	Group A Pimecrolimus	Group B Triamcinolone	Test of Sig.
Age	44.50±6.20 years	45.72±5.35 years	t = -0.633 p = 0.531
Gender	M=11.1%, F=88.9%	M=33.3%, F=66.7%	χ^2 = 2.571 p = 0.109
Morphologic subtype (Erosive/ Cerative)	Yes= 61.1% No= 38.9%	Yes= 72.2% No= 27.8%	χ^2 = 0.50 p=0.480
Erythemaous / atrophic	Yes= 16.7% No= 83.3%	Yes= 5.6% No= 94.4%	χ^2 = 1.125 p = 0.289
Morphologic subtype (Reticular)	Yes= 27.8% No= 72.2%	Yes= 33.3% No= 66.7%	χ^2 = 0.131 p = 0.717
Disease Duration	10.61±6.26 days	16.77±5.49 days	t= -3.138 p = 0.004
VAS pain Score	5.72±2.32	6.77±1.43	t= -1.64 p = 0.110
OHIP Score	3.27±1.17	3.5±1.42	t= -0.150 p = 0.613
Clinical Score	2.38±1.03	2.83±1.15	t= -1.217 p = 0.232

Table No.2: Comparison of the efficacy end points (change from baseline data at each month of the trial), per protocol analysis

Variable	Group A Pimecrolimus	Group B Triamci-nolone	Test of Sig.
Vas Score Pain			
Moth 1, Mean±S.D	5.33±1.37	6.72±1.32	t= -3.09 p = 0.004
Moth 2, Mean±S.D	3.83±1.29	5.33±1.28	t= -3.49 p = 0.001
Moth 4, Mean±S.D	3.22±1.39	4.0±1.57	t= -3.01 p = 0.005
OHIP Score			
Moth 1, Mean±S.D	1.20±0.90	1.26±1.04	t= -0.170 p = 0.866
Moth 2, Mean±S.D	2.10±1.42	2.41±1.23	t= -0.699 p = 0.489
Moth 4, Mean±S.D	1.45±1.03	1.45±1.08	t= 0.000 p = 1.0
Clinical Status Score			
Moth 1, Mean±S.D	0.31±0.18	0.31±0.16	t= 0.095 p = 0.925
Moth 2, Mean±S.D	0.95±0.36	0.79±0.23	t= 1.572 p = 0.125
Moth 4, Mean±S.D	0.58±0.44	0.51±0.53	t= 0.473 p = 0.639

DISCUSSION

Corticosteroids remain first line therapy for symptomatic oral lichen planus, despite of various treatment options, because oral lichen planus is a kind of autoimmune disorder and also because of its effect on connective and epithelial tissues[12]. Topical triamcinolone acetonide has a local anti-inflammatory action and it acts by suppressing T-cell activity[13]. As a result of new searches, a topical immunomodulator i.e. pimecrolimus, with fewer steroids like side effects has been introduced[14]. That is why in this study, pimecrolimus is used to treat symptomatic oral lichen planus.

Lichen planus represents a cell-mediated immune-logical response to a change in the antigen of the mucosa of susceptible individual. That's why immunomodulators and immunosuppressants are used for its treatment. According to the previous studies, use of such agents in oral lichen planus was reported to be efficient and associated with very low number of adverse effects. But reoccurrence was common among the patients after stopping the treatment. Pimecrolimus is a drug of macrolactams group of immunosuppressants just like tarcolimus, which act by T-cell inhibition through calcineurin pathway and inhibition of many other immune related cytokines, thus prevent multiple inflammatory signals. Triamcinolone is more popular in its use for oral lichen planus and previous studies provide solid evidence regarding its efficacy in the treatment of oral lichen planus. Triamcinolone acetonide paste although is preferable to cream and ointment based treatment modalities for lichen planus, there are reports which show that many patients feel uncomfortable with its sticky sensation.

Pimecrolimus is an ascomycin derivative and is a novel drug in dermatologic therapeutics. It was specifically developed to treat inflammatory skin diseases and is one of the drugs in newer classes of immunomodulating macrolactams[15]. The efficacy of pimecrolimus was confirmed after finding its usefulness in treatment of atopic dermatitis and allergic contact dermatitis. Pimecrolimus 1% cream is tolerable and safe even after its repeated topical application in patients with atopic dermatitis as compared to corticosteroids, as it does not result in skin atrophy. The reasons behind substantial interest in pimecrolimus are its considerable anti-inflammatory activity, low systemic immune-suppressive risk and higher immunomodulatory effects[16].

In some studies like by Swift et al[13] Pedraza et al.[17] Taebunpakul et al.[18] Passerron et al[19] Volz et al[20] and McCaughey et al[21] pimecrolimus has shown considerable improvements in all clinical parameters, where it was compared with placebo and showed superior results.

CONCLUSION

According to our study there is significant difference between the efficacy of pimecrolimus cream and triamcinolone acetonide paste, when used for treatment of symptomatic OLP with pimecrolimus cream scoring better than triamcinolone acetonide paste.

Author's Contribution:

Concept & Design of Study:	Hafiz Muhammad Aamir Riaz
Drafting:	Ayesha Shakeel, Maryam Ali Shaheen
Data Analysis:	Ayesha Shakeel, Maryam Ali Shaheen
Revisiting Critically:	Hafiz Muhammad Aamir Riaz, Khurram Jaa
Final Approval of version:	Hafiz Muhammad Aamir Riaz

Conflict of Interest: The study has no conflict of interest to declare by any author.

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