Original Article

Efficacy and Safety of Pimecrolimus Cream (1%) in the Treatment of Discoid Lupus Erythematosus

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Abstract

Discoid lupus erythematosus (DLE) is commonly treated with topical agents, the most important of which are glucocorticosteroids. However, prolonged use of these agents, especially on sensitive areas such as the face, may result in side-effects (e.g. atrophy and telangiectases) by altering collagen synthesis. This was a randomized double-blind pilot study, performed in Department of Dermatology & VD, Ibn-Sina Sina Medical College, Dhaka. Seventy four patients aged 20-53 years with moderate to severe DLE of the face were randomized 8 weeks of treatment and 8 weeks of follow-up after treatment.

In this double-blind study, one group applied pimecrolimus 1% cream twice daily to facial lesions. Efficacy end-points included a combined score based on evaluation of erythema, infiltration and presence of scale. This study was conducted to evaluate the efficacy and safety of topical pimecrolimus 1% cream in discoid lupus erythematosus. It was observed that before treatment, erythema was severe in 43.2% cases, moderate in 51.4% cases and mild type erythema was present in 5.4% cases. The post-treatment revealed, 29.7% severe type erythema, none evidenced moderate type erythema, only 43.2% had mild type and 27% cases no erythema at all. Before treatment, infiltration was severe in 27% cases, moderate in 54.1% cases and only 18.9% had mild type infiltration. But after treatment, 10.8% had severe type infiltration, 18.9% had moderate, 51.4% had mild and 18.9% had no infiltration at all. Similar response to treatment was noticed with squamation which exhibited a drop from 37.8% to 18.9% in severe cases and from 62.2% to 10.8% in moderate cases. There was a 45.9% mild case and 24.3% had no squamous. It was interpreted that score of patients of DLE, before treatment was 6.78±1.36 and after treatment was 3.97±1.21. Improvement was shown in 70.3 cases and 29.73 cases shown no improvement at all. This study suggest that pimecrolimus cream for discoid lupus erythematosus seems to be a safe and clinically effective option. However, this was an open and uncontrolled study, and double-blind, placebo-controlled studies are needed.

Keywords: Discoid Lupus Erythematosus, Pimecrolimus, Infiltration, Erythema.

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Introduction

Discoid lupus erythematosus (DLE) is one of the skin presentations of lupus erythematosus (LE), characterized by the presence of scaly red patches and plaques associated with atrophy[1]. The main goal of treatment in this skin disorder is to improve the appearance of the skin, while preventing disfiguring scars, atrophy or pigmentary alterations[2]. The customary treatment in most cases has been topical therapy, which to some extent can control and occasionally even clear lesions without the need for systemic therapy. Such treatment usually consists of a prolonged course of potent glucocorticosteroids.

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The use of glucocorticosteroids may affect collagen synthesis, resulting in various side-effects, including atrophy and telangiectases,[2,3] thus a better therapeutic alternative is needed.

Topical calcineurin inhibitors (TCIs) are a new generation of immunomodulator therapies, which show promising results in treating inflammatory skin disorders such as atopic dermatitis[4-7]. This family includes ciclosporin, tacrolimus and the newest member, pimecrolimus (Elidel; Novartis Pharmaceuticals, East Hanover, NJ, USA). Several studies have investigated and established the role of tacrolimus in treating DLE[8-14]. The efficacy of pimecrolimus in DLE has not undergone the same scrutiny, but the studies performed to date have shown encouraging results[2,15,16]. This study performed a pilot study to further appraise the efficacy and safety of pimecrolimus as an alternative to more commonly used therapies in treating patients with DLE.

Materials and Methods

This study, a randomized controlled pilot trial, was designed to compare pimecrolimus 1% in the treatment of DLE. All patients were informed about the study procedures and gave their written informed consent. DLE was diagnosed if erythematous, well-defined, scaly plaques, which tended to heal with atrophy and scarring, were present together with histological epidermal atrophy. A precise medical history was obtained and all patients were carefully examined. Biopsy specimens were obtained for histology and direct immunofluorescence, and routine blood tests and complete blood cell count were performed. To ensure no traces of other therapeutic agents (oral and topical steroids, chloroquine, hydroxychloroquine) remained, patients were asked to stop using all topical and systemic treatments at least 4 weeks before the commencement of the trial. The study comprised an 8-week treatment plan plus an 8-week follow-up period. Before patient enrolment, all patients with odd numbers were allocated to patients. Patients were scheduled for follow-up visits at 2-week intervals. Clinical severity score was determined by assessing three factors including erythema, infiltration and presence of scale (0 = normal; 1 = mild; 2 = moderate; 3 = severe)[2,16,19]. Therefore, by adding the scores given to these three independent criteria, the minimum and maximum clinical scores were 0 (normal skin) and 9 (maximum skin damage), respectively, with mild, moderate and severe disease severity defined as scores of 1-3, 4-6 and 7-9, respectively.

Results

Male and female percentage of cases were 21.6 and 78.4 respectively (Table I).

Table-I: Sex distribution of the study subjects (n=74).

Sex	Number	Percentage
Male	16	21.6
Female	58	78.4
Total	74	100.0

It was interpreted that score of patients of DLE, before treatment was 6.78±1.36 and after treatment was 3.97±1.21 (Table II).

Table-II: Mean distribution of before treatment and after treatment (n=74).

Treatment	Mean±SD	P value
Before treatment	6.78±1.36	0.001
After treatment	3.97±1.21	

Erythema was severe in 43.2% cases, moderate in 51.4% cases and mild type erythema was present in 5.4% cases.The post-treatment scenario revealed- 29.7% severe type erythema, none evidenced moderate type erythema , only 43.2% had mild type and 27% cases no erythema at all (Table III).

Table-III : Grading of erythema before and after treatment (n=74).

	Before treatment		After treatment	
	No	%	No	%
Normal	0	00	20	27
Mild	4	5.4	32	43.2
Moderate	38	51.4	0	00
Severe	32	43.2	22	29.7

Before treatment, infiltration was severe in 27% cases, moderate in 54.1% cases and only 18.9% had mild type infiltration. But after treatment, 10.8% had severe type infiltration, 18.9% had moderate, 51.4% had mild and 18.9% had no infiltration at all (Table IV).

Table-IV: Grading of infiltration before and after treatment (n=74).

	Before treatment		After treatment	
	No	%	No	%
Normal	0	00	14	18.9
Mild	14	18.9	38	51.4
Moderate	40	54.1	14	18.9
Severe	20	27.0	8	10.8

Squamation exhibited a drop from 37.8% to 18.9% in severe cases and from 62.2% to 10.8% in moderate cases. There was a 45.9% mild case and 24.3% had no squamation (Table V).

Table-V: Grading of squamation before and after treatment (n=74).

	Before treatment		After treatment	
	No	%	No	%
Normal	0	00	18	24.3
Mild	0	00	34	45.9
Moderate	46	62.2	8	10.8
Severe	28	37.8	14	18.9

Improvement was shown in 70.3 cases and 29.73 cases shown no improvement at all (Table VI).

Table-VI: Percentage of improvement of the study subjects (n=74).

	Number	Percentage	P value
Improved	52	70.3	
Not improved	22	29.7	0.001
Total	74	100.0	

Discussion

In recent years, treatment of DLE worldwide has been mainly restricted to the use of mid-potency to high-potency topical glucocorticosteroids. Prolonged use of these drugs can lead to a number of side-effects, including atrophy or thinning of the skin, telangiectasia, or rarely, systemic adrenal suppression[2,3]. Calcineurin inhibitors, do not have these adverse effects, and the main side-effects reported with these drugs have been a local burning sensation and pruritus[17,18].

The present study trials the effects of pimecrolimus 1%. At the end of the 8-week treatment the clinical severity score showed a substantial improvement, which was confirmed by statistical analysis.

The main reason for developing new drugs as an alternative to topical steroids is to overcome side-effects, such as thinning of the skin and adrenal gland suppression, and recent studies have demonstrated that skin thinning is avoided with the use of pimecrolimus cream[19]. This pilot study demonstrates that pimecrolimus 1% cream as monotherapy was effective in the amelioration of the skin score of patients of DLE, before treatment was 6.78 ± 1.36 and after treatment was 3.97 ± 1.21 (P = 0.001). The safety profile in this open trial is similar to those reported in previous atopic dermatitis clinical trials[20]. Zabawski[21] was the first to describe, in a single case report, a moderate improvement of DLE lesions under pimecrolimus ointment; however, he did not mention the schema employed, the duration of treatment or the method of assessing improvement. More recently, Kreuter et al.[22] reported on topical pimecrolimus in 11 patients with different forms of cutaneous lupus, including four patients with DLE, three with SLE, two with subacute cutaneous and two with lupus tumidus. The patients were treated with pimecrolimus twice daily, and the evening applications were followed by overnight occlusion with hydrocolloid dressings to increase the cutaneous uptake of the cream. Significant amelioration of the skin lesions was observed after therapy. Interestingly, the overall percentage of improvement was very similar 74% in this study, but without using overnight occlusion.

A few studies in DLE have included the analysis of QOL; this aims to measure objectively how the patient's life is affected by the disease[23]. Skindex-29 is a generic and widely validated instrument to measure QOL in patients with skin diseases [17]. Therefore we employed the Spanish version of Skindex-29, which had demonstrated validity, reliability and sensitivity to change, which is an specially important issue for drug evaluation trials[18]. Systemic side-effects are absent with topical pimecrolimus, but topical side-affects include burning sensation, tingling, flushing and folliculitis at the application site[24].

In our study 51.4% had moderate erthema in before treatment and after treatment shows had no moderate erythema. 43.2% were severe erythema in before treatment and 29.7% were severe in after treatment. Therefore, the findings of the study are in well agreement with the findings of the other research works[2,3].

Our data suggest that pimecrolimus 1% cream for DLE seems to be a safe and clinically effective option, especially for resistant DLE at sensitive sites such as the face, where the use of potent topical steroids carries a high risk of thinning of the skin and telangiectasia. However, the place of pimecrolimus in the treatment of cutaneous lupus will depend on its efficacy when compared with established topical treatments, such as corticosteroids. The present study had an open-label design and involved only a small number of patients and no control group, therefore double-blind, placebo controlled studies are needed in order to confirm our data. This work was supported in various other studies conducted across India[13,14].

There were few side-effects in the pimecrolimus this could be due to the limited exposure time to these medications. In addition, despite the improvement lasting for 8 weeks observed in our patients, we cannot draw any conclusions on the efficacy of pulsed topical treatments because of the limited number of patients and followup period. Our trial, moreover, did not include a placebo control group.

Conclusion

It was observed that pimecrolimus is a good alternative for corticosteroids in dealing with the scaly and atrophic patches found in discoid lupus erythematosus. Further studies on larger groups of patients are needed.

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