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ORIGINAL ARTICLE

Efficacy of the topical cyclosporine cream assisted by fractional carbon dioxide laser vs topical clobetasol cream for the treatment of plaque psoriasis: Randomized comparative study

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Abstract

Background: In mild psoriasis, topical agents remain the mainstay of treatment. However, the available treatments are not satisfactory for a significant proportion of patients in many terms such as efficacy and safety. Because of these deficits, augmentation of therapeutic effect seems desirable.

This study aims: To evaluate the efficacy of topical cyclosporine cream, delivered by fractional CO_2 laser vs the efficacy of topical clobetasol cream for the treatment of mild to moderate plaque psoriasis.

Patients and methods: Twenty-two patients with chronic plaque psoriasis involving <10% BSA were included in this study. They were randomly allocated into 2 groups. In Group A, patients were instructed to apply cyclosporine cream twice daily for 5 consecutive days per week immediately after fractional carbon dioxide laser session. While in Group B, clobetasol cream was applied twice daily for 5 consecutive days per week until complete clearance or for a maximum of 10 weeks.

The efficacy was objectively assisted clinically and by histopathology by using the scores and skin biopsy.

Results: There was a significant improvement of erythema, plaque elevation, and scaling ($p < 0.001$) with the use of topical cyclosporine cream delivered by the aid of fractional CO_2 laser, compared to base line. However, the improvement was more significant with topical clobetasol cream.

Conclusion: Laser-assisted delivery of topical cyclosporine can provide comparable clinical and pathological improvement to that of clobetasol in the psoriatic plaques. These findings were apparent in patients with less widespread disease. However, topical steroid showed more improvement.

KEYWORDS
clobetasol cream, laser-assisted drug delivery, plaque psoriasis, psoriatic itch, topical cyclosporine

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1 | INTRODUCTION

Psoriasis is a chronic inflammatory skin disease associated with multiple comorbidities and significantly diminishes patients' quality of life.[1] It has a worldwide prevalence of 0.09%–5.1%.[2]

Psoriasis has several clinical presentations. The most common form of psoriasis, occurring in 85%–90% of patients, is plaque-type psoriasis. It is characterized by well-demarcated, scaly, and erythematous, infiltrated plaques. On the microscopic level, keratinocytes proliferate rapidly at high turnover rates leading to incomplete terminal differentiation. Abnormal differentiation causes epidermal thickening (acanthosis), retention of keratinocyte nuclei within the stratum corneum cells (parakeratosis), and loss of the granular layer. Neutrophils accumulate within the epidermis forming Munro's micro-abscesses. Psoriatic lesions are highly vascular and densely infiltrated by T cells and dendritic cells (DC) which are key players in its pathophysiology.[3]

Patients can experience substantial pruritus with moderate to severe psoriasis or during exacerbation1. However, recent studies demonstrated that approximately 60%–90% of patients with psoriasis have pruritus and they consider it as one of the most bothersome symptoms of their disease.[4] Unfortunately, due to the delay in recognizing the severity of pruritus in psoriasis, the development of therapeutic options has been delayed.[5]

Numerous studies have focused on the pathogenesis concerning this disease therefore improving the therapeutic approaches.[6]

Management of psoriasis is related to the extent of the skin involvement. Treatment goals include improving and controlling physical signs if possible, improving secondary psychological effects, reducing inflammation, and controlling skin shedding. Approaches are generally individualized because of the variable presentation, quality of life implications, and co-existent medical conditions. Individual responses and commitments to therapy also present possible limitations.[7]

For patients with mild psoriasis, topical agents are the mainstay of treatment, as topical corticosteroids, vitamin D analogues, calcineurin inhibitors, and keratolytic.[1]

The American Academy of Dermatology-National Psoriasis Foundation guidelines recommend biologics as an option for first-line treatment of moderate to severe plaque psoriasis due to their efficacy in treating it and acceptable safety profiles.[1]

Oral treatments include methotrexate, acitretin, cyclosporine, and apremilast, which is a phosphodiesterase 4 inhibitor. The most used light therapy is narrowband UV-B phototherapy.[1]

Oral administration of cyclosporine is indicated in the treatment of severe recalcitrant plaque psoriasis. However, cyclosporine is both nephro- and hepatotoxic and its systemic administration exposes the patient to other severe side effects. Although topical delivery of cyclosporine, targeted directly to psoriatic skin, would offer significant advantages, there are no topical formulations approved for dermatological use.[8]

The concept of fractional laser-assisted drug delivery has now been taken into clinical practice to enhance uptake of topical therapeutics and improve clinical outcomes for certain skin conditions.[9]

Laser-assisted drug delivery (LADD) offers the potential advantages of reduced treatment durations and the replacement of cumbersome, patient-dependent treatment regimens with quick, in-office procedures. With continuous development, however, LADD promises to improve existing regimens and make new pharmacological treatments a reality for a wide range of cutaneous disorders.[10]

This study aims to evaluate the efficacy of topical cyclosporine cream when delivered by fractional carbon dioxide laser in comparison to the efficacy of topical clobetasol cream for the treatment of mild to moderate plaque psoriasis.

2 | PATIENTS AND METHODS

Twenty-two patients with chronic plaque psoriasis involving >10% body surface area (BSA) were included in this randomized, comparative study and were randomly allocated, using sealed envelopes, into 2 groups: A and B. Eleven patients in each group. sample size was properly calculated to have statistically significant or non-significant values based on the clinical objective assessment and histological variables.

Signed consent was obtained from each patient before enrollment. The study was conducted according to the Declaration of Helsinki principles and was approved by the ethical committee of national laser institutional review board (EC Ref NO 019–012).

Pregnant, lactating women, and children were excluded. Also, patients with concomitant renal, hepatic, and hematological abnormalities were excluded.

A pre-study washout period of 4 weeks to eliminate the consequences of previous topical therapy and 2 months for systemic or ultraviolet therapy was followed up.

2.1 | Preparation of test material

Materials used included marketed clobetasol propionate 0.05% cream (dermovate SmithKline Beecham, under license from GalaxoWellcome Limited), marketed cyclosporine 100 mg caps (Sandimmun Neoral 100 mg oral capsules, (novatis pharma AG, Basilea Suiza)), and petrolatum jelly (Vaseline original, unilever, UAE).

The topical cyclosporine cream utilized in this study was prepared in the pharmaceutical department of National Institute of Laser Enhanced Sciences. Sandimmun Neoral 100 mg oral capsules were used. Each 100 mg blue gray oblong shaped soft gelatin capsule contains nearly 0.9 ml of clear faintly yellow solution of micro-emulsion preconcentrate containing 100 mg cyclosporine as an active ingredient and lots of excipients like alpha tocopherol, corn oil, and hydrogenated castor oil. The content of 6 capsules was extracted and mixed with 80 ml sterile petrolatum gel base under stirring till complete dispersion, then the quantity was completed to 100 ml to form 5% v/v topical-cyclosporine cream.

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Cyclosporine cream was tested for repeated insult patch test on a healthy area of the back of each patient to assess the potential irritation of the skin[11]. Also, patients were asked to report any delayed reaction which may occur after the challenge skin test.

2.2 | Instrument

Fractional CO_2 laser (Deka Smartxide Italy, code M079S1).

The parameters used were: 8 joules Fluence of scanning mode, stack 1, rectangular pulse shape, scanning dwell time of 600ųs, spacing of 250 ųm, and every lesion was exposed to one laser pass.

2.3 | Treatment protocol

Group A: Each patient was instructed to use cyclosporine cream twice daily over their psoriatic lesions for 5 consecutive days per week immediately after fractional CO_2 laser session. The laser sessions were done on weekly intervals until complete clearance or for a maximum of 10 laser sessions. While in Group B patients, clobetasol cream was applied twice daily for 5 consecutive days per week until complete clearance or for a maximum of 10 weeks. The efficacy of the treatment was evaluated every 2 weeks. The study was concluded at the end of 12 weeks.

2.4 | Evaluation methods

Objectively, the severity of psoriasis was evaluated using Psoriasis Area Severity Index (PASI) described by Fredriksson and Pettersson.[12] Target Lesion Psoriasis Severity Scale (TLPSS) was used to measure improvement of the individual lesion.[13] Global assessment was made by two blinded physicians to assess the result of therapy (on a scale of 0–5). A score of 5 indicates worsening of lesion and score 0 indicates complete clearance of lesion.[14] Also, pruritus was evaluated employing a pruritus severity score.[15]

Histopathologic evaluations were achieved by 4 mm punch biopsies, that were taken before and at the end of 12 weeks. Each biopsy stained with hematoxylin & eosin for histopathological study. Measurements were taken by Leica Qwin software version 3, Leica Microsystems, Switzerland. Images were captured using Digital camera Leica model DFC295 & Light microscope Leica model DM LB2 (Switzerland), different magnification powers were used for proper visualization and measurements. Biopsy was taken 2 weeks after remission induction if that lesion has complete remission before 12 weeks.

Subjectively, the patients were asked to assess treatment satisfaction at the end of the study on a 4-point scale (very satisfied, satisfied, disappointed, or very disappointed). The patients were asked about the reasons for their grading of satisfaction.[16]

This study did not measure serum creatinine or serum level of cyclosporine as it selected a small area (less than 10% BSA); hence, there were no significant concerns regarding systemic absorption.

TABLE 1 Demographic data of the patients

Characteristics	Lase/Cyclosporine group	Clobetasol group
Age	47.54 ± 11.76	44.36 ± 11.01
Duration	11.91 ± 6.56	11.00 ± 5.81
Gender		
Male	6 (54.54%)	8 (72.80%)
Female	5 (45.46%)	3 (27.30%)
Skin Type		
III	8 (72.80%)	7 (63.60%)
IV	3 (27.30%)	4 (36.40%)
Plaque Location		
Elbow—Forearm	11 (100%)	10 (90.90%)
Knee—Legs	11 (100%)	11 (100%)
Lower Back	5 (45.46%)	4 (36.40%)
PASI Score Before	5.67 ± 0.88	5.40 ± 0.97
TLPSS Score Before	9.45 ± 1.46	9.00 ± 1.62

Note: Demographic data and lesions' locations before the treatment.

2.5 | Statistical analysis

Data were analyzed using computer programs: Microsoft Excel and Statistical Program for Social Science (SPSS) version 21. Quantitative data were expressed as mean ± SD and qualitative data were expressed as frequency and percentage. Independent samples *t*-test of significance was used when comparing two means. Paired samples *t*-test of significance was used when comparing related samples. Chi-square test of significance was used to compare proportions of two qualitative parameters. Probability (*p*-value) <0.05 was considered significant, *p*-value <0.001was considered as highly significant, and *p*-value >0.05 was considered insignificant.

3 | RESULTS

This was a randomized study. The 22 study participants had been randomly allocated into 2 groups. The demographic data are in (Table 1).

Mean PASI scoring for group A and B patients before introduction of the treatment were (5.67 ± .88) and (5.40 ± .97), respectively. Mean TLPSS was (9.45 ± 1.46) in group A and (9.00+1.62) in group B.

Both treatments were significantly effective in management of the psoriatic plaques so they could be compared with each other. However, topical steroid showed more improvement * = significant $p < 0.05$ ** = highly significant $p < 0.01$. There was a significant improvement of erythema, plaque elevation, and scaling ($p < 0.001$) with the use of topical cyclosporine cream delivered by the aid of fractional CO_2 laser as compared to base line. However, the improvement was more significant with topical clobetasol

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TABLE 2 Mean of scores and PGA score

Variable	Laser And Cyclosporine Before	Laser And Cyclosporine After	Clobetasol Before	Clobetasol After
Mean of scores				
Erythema	3.77 ± 0.63	1.36 ± 0.78*	2.91 ± 0.68	0.09 ± 0.29**
Induration	3.00 ± 0.75	1.00 ± 0.87**	3.09 ± 0.68	0.09 ± 0.29**
Scale	3.18 ± 0.95	1.00 ± 0.87**	3 ± 0.75	0.36 ± 0.49**
TLPSS	9.45 ± 1.46	3.00 ± 2.21*	9.00 ± 1.62	0.55 ± 0.90**
PASI score	5.67 ± 0.88	2.02 ± 1.31*	5.40 ± 0.97	0.33 ± 0.54**
Pruritus score	7.45 ± 1.58	3.27 ± 1.31**	7.27 ± 1.63	2.45 ± .39**
PGA score				
0 Clear	0%	1 (9.10%)	0%	7 (63.60%)
1 Almost Clear	0%	3 (27.30%)	0%	3 (27.30%)
2 Mild	0%	3 (27.30%)	0%	1 (9.10%)
3 Moderate	0%	4 (36.40%)	2 (18.20%)	0%
4 Moderate to severe	2 (18.20%)	0%	7 (63.60%)	0%
5 Severe	9 (81.80%)	0%	2 (18.20%)	0%
Mean score	4.82 ± 0.39	1.91 ± 1.01*	4 ± 0.61	0.45 ± 0.67**

Note: * = significant $p < 0.05$ ** = highly significant $p < 0.01$

cream. (Table 2). Test Statistics in study groups are shown in (Table 3).

The average time needed for remission induction was 7 weeks in group A but 4 weeks in group B.

In cyclosporine group, (A) marked improvement was elicited in the induration and scaling, while erythema showed moderate improvement (Table 2, Figure 1A,B). In steroid group, (B) scale parameter showed least improvement (Table 2, Figure 2A,B).

Regarding improvement on PASI scoring its mean reduced by 3.65 points in cyclosporine group while in steroid group it reduced by 5.07 points.

From a mean baseline TLPSS of 9.45 in group A and 9 in group B sum of scores, improved by an average of 6.45 points after a period of 10 weeks of cyclosporine cream, compared with 8.45 points in steroid group (Table 2, Figure 1,2).

The Physician Global Assessment (PGA) score of clear or almost clear was reached at 36.40% in group A, compared with 90.90% in group B (Table 2). Two independent physicians used TLPSS to assess improvement of individual psoriatic lesions.

Itching improved in both groups. From a mean baseline score of 7.45 in group A and 7.27 in group B on a standard 10-point pruritus visual analog scale, cyclosporine treated areas showed a mean 4.18-point decrease compared with a 4.82-point reduction in steroid-treated areas.

In group A the majority (72.72%) of the patients reported to be very satisfied (45.45.0%) or satisfied (27.27%) after the topical cyclosporine treatment delivered by fractional Co2. Disappointments were reported by 27.28% of the patients. While in group B all patients (100%) reported to be very satisfied (90.90%) or satisfied (9.10%) with the use of clobetasol cream.

Efficacy, tolerability, and ease of use were the main reasons for the patients' satisfaction in both groups. Disappointment was related to incomplete clearance of psoriatic lesions and to a lesser extent because of burning pain in group A.

Regarding histopathological evaluation that showed section for skin biopsy taken before treatment by a 4 mm punch and stained with (H&E). Histopathological examination revealed: hyperkeratosis thickness (1850.21 ± 30.06) with intermittent parakeratosis, regular elongation of the rete ridges (mean length 569.98 ± 23.86), edema and elongation of the dermal papillae (mean length 430.25 ± 1.50), thinning of the supra-papillary plate (mean thickness 37.45 ± 3.66), absent granular cell layer, dilated blood vessels, and perivascular and dermal infiltrates of lymphocytes.

Findings showed improved pathological features with topical cyclosporine treatment, normalization of stratum corneum thickness (mean 230.47 ± 17.82), restoration of granular layer and orthokeratosis, normal supra-papillary plate (mean thickness 46.23 ± 5.11), normal length of rete ridges and dermal papillae (their means 244.91 ± 0.74 and 223.61 ± 24.05, respectively), no dermal edema and reduction in lymphocytes infiltrate. (Table 4).

Histological findings showed improved pathological features with topical clobetasol cream, normalization of stratum corneum thickness (mean 237.42 ± 13.74), restoration of granular layer and orthokeratosis, normal supra-papillary plate (mean thickness 39.62 ± 1.49), normal length of rete ridges and dermal papillae (their means 226.62 ± 13.84 and 121.02 ± 19.17, respectively), no dermal edema, and reduced lymphocytes infiltrate. (Table 4) No patient in both groups showed a flare during washout period. infections were seen at the treated sites during the study period in both groups.

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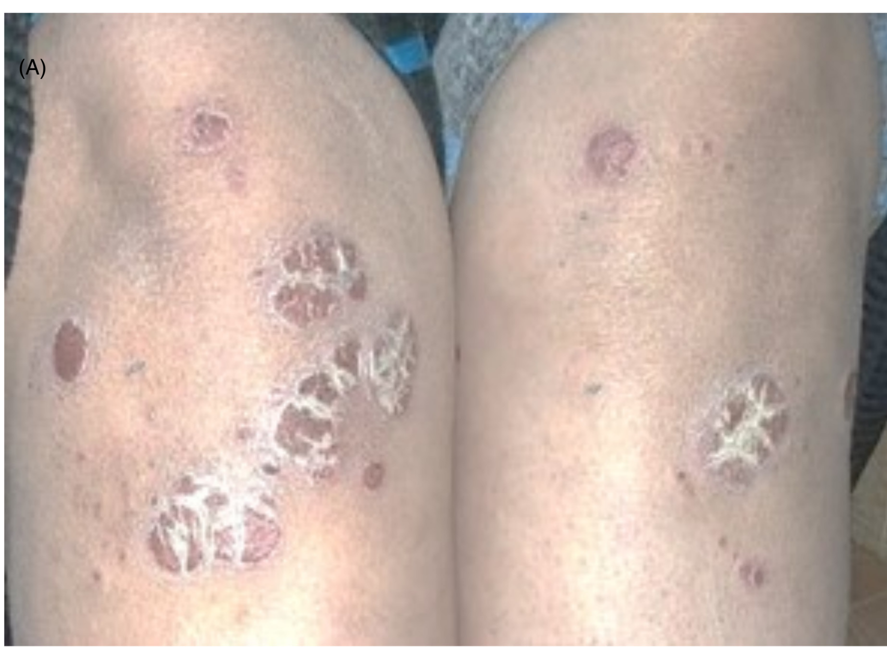
TABLE 3 Test Statistics in study groups

Test Statistics							
* Group A vs **Group B after treatment	Erythema	Induration	Scale	PASI score	PRURITUS	TLPSS	PGA
Z	−4.657[b]	−3.874[b]	−3.021[b]	−4.056[b]	−2.441[b]	−4.009[b]	−4.203[b]
Asymp. Sig. (2-tailed)	.000	.000	.003	.000	.015	.000	.000
A. Wilcoxon signed rank test							
B. Based on positive ranks.							

Note: * = significant $p < 0.05$ ** = highly significant $p < 0.01$



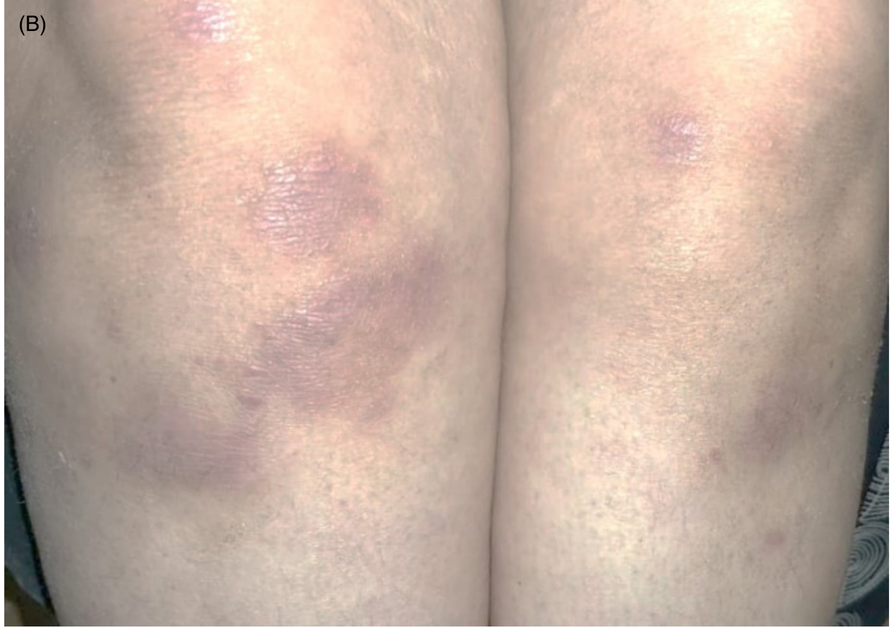


FIGURE 1 (A) Psoriatic plaques (bilateral knee). (B) Almost cleared psoriatic plaques with LADD of cyclosporine with remnant mild erythema (bilateral knee)

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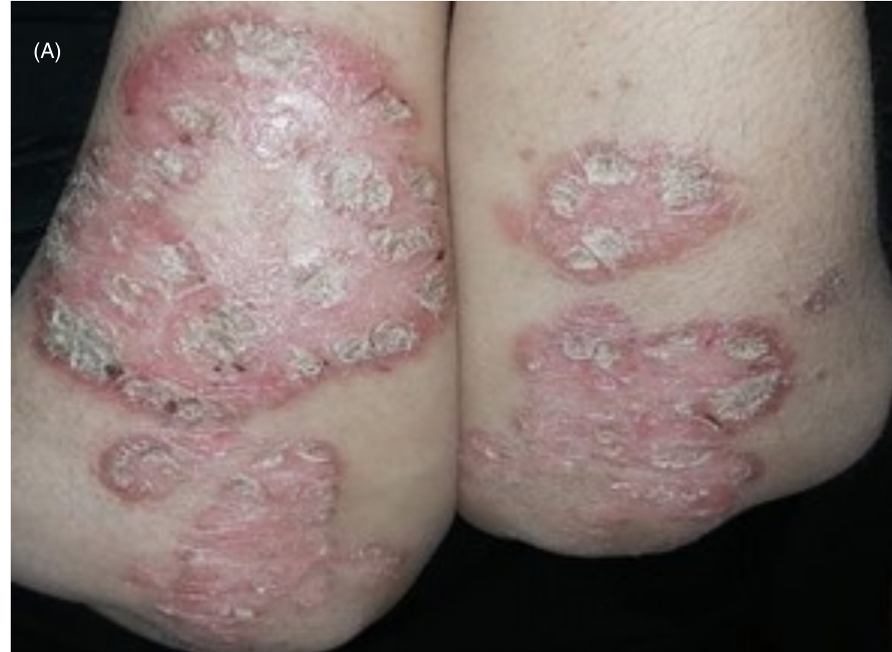

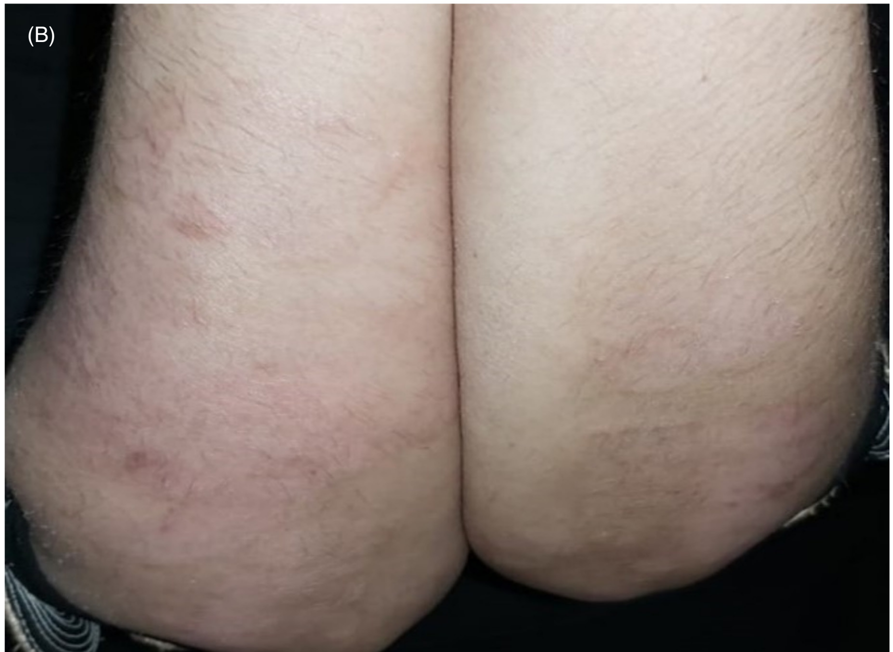

FIGURE 2 (A) Psoriatic plaques (bilateral elbow). (B) Almost cleared psoriatic plaques with topical clobetasol with remnant fine scales (bilateral elbow)

TABLE 4 histopathological measurements

Histopathological measurements Mean ± SD	Before treatment	After treatment	
		(Group A) laser & cyclosporine	(Group B) clobetasol
Hyperkeratosis thickness (40X)	1850.21 ± 30.06	230.74 ± 14.82**	237.42 ± 13.74**
Rete ridges length (100X)	569.98 ± 23.86	244.91 ± 0.74**	226.62 ± 13.84**
Dermal papillae length (100X)	430.25 ± 1.50	223.61 ± 24.05**	121.02 ± 19.17**
Supra-papillary plate thickness (100X)	37.45 ± 3.66	46.23 ± 5.11**	39.62 ± 1.49**
Perivascular lymphocyte number /HPF (400X)	9	6	8

Note: * = significant $p < 0.05$ ** = highly significant $p < 0.01$

4 | DISCUSSION

Psoriasis is a chronic skin disease with no known cure currently. However, the severity of psoriasis can oscillate over time, and its symptoms can be effectively controlled with treatments.[1]

The results of this study demonstrated that the use of fractional CO_2 laser could play a role in the enhancement of the delivery of the cyclosporine preparation. It provides clinical and pathological improvement in the psoriatic plaques in patients with less widespread disease while minimizes the risk of systemic exposure.

Interestingly, LADD allows for selective targeting of the skin by delivering the topical therapeutic agent to the depth of the dermo-epidermal junction, a critical region where inflammatory cells cross to promote disease progression.[17]

A preliminary study confirmed that fractional laser ablation can be used for the cutaneous delivery humanized anti-CD29 monoclonal antibody to enable the targeted use of a biologic for the treatment of recalcitrant psoriatic plaques in patients with less widespread disease.[17]

Also, cutaneous bio distribution studies demonstrated that Etanercept was delivered in therapeutically relevant amounts to the epidermis and dermis by using laser-assisted delivery.[18]

Clearly, these results showed that both drugs improve psoriatic plaques; however, steroid showed more improvement, and this was expected as topical calcineurin inhibitors are equal to class IV-VII steroids, while clobetasol is the strongest potency (superpotent).[1]

Evidently, topical cyclosporine preceded by fractional laser showed marked improvement of scales followed by induration, then erythema as laser ablation removes excess scales and the inhibitory effect of cyclosporine on keratinocyte proliferation maintains this result of decreased scaling.[19] Also, cyclosporine has the capacity to modulate differentiation of the keratinocytes decreasing production of parakeratotic cells within the stratum corneum which is responsible for the silvery appearance of scales.[20] Cyclosporine can modulate inflammation, cellular-mediated immune response, and angiogenesis.[21] All these findings are in total agreement with this study's findings.

Topical Steroid showed marked improvement of erythema followed by induration then scales. This was attributed to its anti-inflammatory, locally vasoconstrictive effects via downregulation of genes coding proinflammatory cytokines and antiproliferative effect.[1]

PASI scoring, for cases treated by cyclosporine, showed complete clearance of their disease in 9.10% but 90.90 of patient became mild degree. In the steroid group, 63.60% showed complete clearance of their disease and 36.40% had a mild degree of the disease. this improvement was sustained for a 6 weeks follow-up post study period in both groups.

This study's results were in close agreement when compared with Kumar R et al,[22] who found complete clearance (ie, DSS = 0) in 41% psoriasis lesioned sites treated with cyclosporine lipogel and 85.7% of sites treated with clobetasol propionate cream. The difference in percentage of improvement might be attributed to a different method of formulation and delivery. In this study, authors used 5% v/v delivered by fractional laser while Kumar et al used 2% w/w delivered by liposome.

Basically, histopathological examination of psoriatic lesions is a more objective measure of response than assessment of PASI. In this study, clinical improvement of plaque severity was proved histologically on examination of biopsies taken after treatment, that showed reduced epidermal hyperplasia, restoration of a granular layer and orthokeratosis, and normalization of rete ridges and dermal papillae lengths. These changes and normalization of K16 expression were defined as histologic remission.[3] Findings were translated clinically into reduced plaque elevation, reduces scaling and decreased visibility of erythema.

Importantly, a well-known factor contributing to the pathogenesis of psoriasis is abnormal keratinocyte proliferation.[23] Furthermore, the invasion of nerve endings occurs within the epidermis. In these study cases, the initial site of itch (ie, nerve endings of peripheral sensory neurons) is likely to be adjacent to the layer of keratinocytes. Therefore, the contribution of keratinocytes to itch in psoriasis is significant with associated inflammation and hyperproliferation of epidermal cells.[24,25]

As cyclosporine has an inhibitory effect on keratinocyte proliferation, in addition to the inhibition of cytokine secretion and decreased inflammatory infiltrate, it also inhibits the release of mast cell mediators, and downregulates cellular adhesion molecule expression on the capillary endothelium of dermal blood vessels which provides an antipruritic effect.[5,26]

Frequently, many modalities are emerging in each single specialty,[27] and many modalities for the management of psoriasis have been tried[28–30] and this study is one of these modalities for a possible better approach in the treatment.

In this study, improved pruritus and lesion visibility might be the major contributions in patient's satisfaction in addition to safety concerns.[31] So improved plaque severity and the decreased pruritus with topical cyclosporine would improve patient's quality of life suggesting that this treatment method would be clinically useful. Findings in this study showed that pruritus responded rapidly in both groups. Its mean score decreased by 4.18 points in the cyclosporine group compared to a 4.82 point reduction in the steroid group.

This study showed mild burning/stinging lasted for 24–48 h where treatment-related adverse events were noticed in 2 patients of group A. These findings are probably related to laser-induced thermal trauma and the selective photo-thermolysis which is the mainstay theory for laser penetration.[32] Laser sessions were done weekly to keep micro-channels present for the aid of drug permeation.

These findings open a new research cycle for further studies to assess relapse rates and safety on long-term use. It recommends further studies to evaluate efficacy and safety in certain locations, such as face and flexural areas, as well as to develop suitable formulation to be used for scalp psoriasis.

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5 | CONCLUSION

Laser-assisted delivery of topical cyclosporine can provide clinical and pathological improvement in the psoriatic plaques. These findings were apparent in patients with less widespread disease. However, topical steroid showed more improvement.

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CONFLICT OF INTEREST

The authors declare that they have no conflict of interest either direct or potential and have no fund or financial support.

AUTHORS' CONTRIBUTION

All Authors have shared the article processing stages especially data interpretation, results analysis, and discussion. First Author has revised and approved the final form of the article to be published. The second till the fifth authors have contributed to conception and design, acquisition of data, analysis, and interpretation of data.

DISCLOSURE

This Paper has not been published in any other journal, neither is it presented in any meeting. All authors have approved the manuscript and agree with submission to your journal. The authors have no conflicts of interest to declare.

ETHICAL STATEMENT

The authors confirm that the ethical policies of the journal, as noted on the journal's author guidelines page, have been adhered to and the appropriate ethical review committee approval has been received.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are openly availableon simple request to the authors.

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REFERENCES

1. Armstrong AW, Read C. Pathophysiology, clinical presentation, and treatment of psoriasis: a review. *JAMA*. 2020;323 (19):1945-1960.
2. Michalek IM, Loring B, John SM. A systematic review of worldwide epidemiology of psoriasis. *J Eur Acad Dermatol Venereol*. 2017;31:205-212.
3. Benezeder T, Wolf P. Resolution of plaque-type psoriasis: what is left behind and reinitiates the disease. *Semin Immunopathol*. 2019;41:633-644.
4. Szepietowski JC, Reich A. Pruritus in psoriasis: an update. *Eur J Pain*. 2016;20:41-46.
5. Komiya E, Tominaga M, Kamata Y, Suga Y, Takamori K. Molecular and cellular mechanisms of itch in psoriasis. *Int J Mol Sci*. 2020;21(21):8406.
6. Ardeleanu V, Radaschin D, Tatu A. Excimer laser for psoriasis treatment: a case report and short review. *Exp Ther Med*. 2020;20(1):52-55.
7. Medical Advisory Secretariat. Ultraviolet phototherapy management of moderate-to-severe plaque psoriasis: an evidence-based analysis. *Ont Health Technol Assess Ser*. 2009;9(27):1-66.
8. Lapteva M, Santer V, Mondon K, et al. Michael möller 1, yogeshvar n kalia targeted cutaneous delivery of ciclosporin A using micellar nanocarriers and the possible role of inter-cluster regions as molecular transport pathways. *J Control Release*. 2014;28(196):9-18.
9. Haedersdal M, Erlendsson AM, Paasch U, Anderson RR. Translational medicine in the field of ablative fractional laser (AFXL)-assisted drug delivery: a critical review from basics to current clinical status. *J Am Acad Dermatol*. 2016;74(5):981-1004.
10. Wenande E, Erlendsson AM, Haedersdal M. Opportunities for laser-assisted drug delivery in the treatment of cutaneous disorders. *Semin Cutan Med Surg*. 2017;36(4):192-201.
11. Tardiff RJ, Hubner RP, Graves CG. Harmonization of thresholds of primary skin irritation from results of human repeated insult patch tests and laboratory animal skin irritation tests. *J Appl Toxicol*. 2003;40:464-467.
12. Fredriksson T, Pettersson U. Severe psoriasis: oral therapy with a new retinoid. *Dermatologica*. 1978;157:238-244.
13. Patel RV, Tsui CL. Evaluating psoriasis: a review of the assessments most commonly used in clinical trials. *Psoriasis Forum*. 2011;17a(4):259–266. https://doi.org/10.1177/247553031117a00403
14. Freedman JD, Gottlieb AB, Lizzul PF. Physician performance measurement: tiered networks and dermatology (an opportunity and a challenge). *J Am Acad Dermatol*. 2011;64(6):1164-1169. https://doi.org/10.1177/247553031117a00403
15. Erickson S, Kim BS. Research techniques made simple: itch measurement in clinical trials. *J Invest Dermatol*. 2019;139(2):264-269.
16. Claréus B, Houwing R, Sindrup J, Wigchert S. The DESIRE study - Psoriasis patients' satisfaction with topical treatment using a fixed combination of calcipotriol and betamethasone dipropionate in daily clinical practice. *Eur J Dermatol*. 2009;19:581-585. https://doi.org/10.1684/ejd.2009.0767
17. Lapteva M, del Río-Sancho S, Wu E, Carbonell WS, Böhler C, Kalia YN. Fractional laser ablation for the targeted cutaneous delivery of an anti-CD29 monoclonal antibody – OS2966. *Sci Rep*. 2019;9(1):1030.
18. del Río-Sancho S, Lapteva M, Sonaje K, et al. Targeted cutaneous delivery of etanercept using Er:YAG fractional laser ablation. *Inter J Pharm*. 2020;580:119234.
19. Samarasekera EJ, Sawyer L, Wonderling D, Tucker R, Smith CH. Topical therapies for the treatment of plaque psoriasis: systematic review and network meta-analyses. *Br J Dermatol*. 2013;168(5):954-967.
20. Murphy M, Kerr PH, Grant-Kels JM. The histopathologic spectrum of psoriasis. *Clin Dermatol*. 2007;25:524-528.
21. Maza A, Montaudié H, Sbidian E, et al. Oral cyclosporin in psoriasis: a systematic review on treatment modalities, risk of kidney toxicity and evidence for use in non-plaque psoriasis. *J Eur Acad Dermatol Venereol*. 2011;25(suppl. 2):19-27.
22. Kumar R, Dogra S, Amarji B, et al. Efficacy of novel topical liposomal formulation of cyclosporine in mild to moderate stable plaque psoriasis: a randomized clinical trial. *JAMA Dermatol*. 2016;152:807-815.
23. Greb JE, Goldminz AM, Elder JT, et al. Psoriasis. *Nat Rev Dis Primers*. 2016;2:16082.

14732165, 2022, 8, Downloaded from https://onlinelibrary.wiley.com/doi/10.1111/jocd.14595 by Egyptian National Sti. Network (Enstinet), Wiley Online Library on [15/05/2024]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

24. Takahashi N, Tominaga M, Kosaka R, et al. Involvement of _-opioid receptors and _-opioid receptors in itch-related scratching behaviour of imiquimod-induced psoriasis-like dermatitis in mice. *Acta Derm Venereol*. 2017;97:928-933.
25. Ghazy A, Sadek A, Kamel A, Tahoun A. Serum clusterin in psoriasis: relation to metabolic syndrome. *Al-Azhar Inter Med J*. 2020;1(7):64-68. https://doi.org/10.21608/aimj.2020.30442.1232
26. Ko K, Tominaga M, Kamata Y. et al. Possible antipruritic mechanism of cyclosporine a in atopic dermatitis. *Acta Derm Venereol*. 2016;96(5):624-629.
27. Ali YH, Al Sheikh AE. Nonmicrosurgical grafting for facial nerve branches with permanent sensational functional outcome. *Plast Reconstr Surg Glob Open*. 2019;7(5):e2195. https://doi.org/10.1097/GOX.0000000000002195. Published 2019 May 16.
28. Khattab F, Samir MA. Botulinum toxin type-A versus 5-fluorouracil in the treatment of plaque psoriasis: comparative study. *J Cosmet Dermatol*. 2021;20(10):3128-3132.
29. Botsali A, Erbil H. Management of nail psoriasis with a single injection of abobotulinum toxin. *J Cosmet Dermatol*. 2021;20(5):1418-1420. https://doi.org/10.1111/jocd.13633. Epub 2020 Aug 11 PMID: 32783318.
30. Hemida AS, Hammam MA, Salman ATA, Shehata WA. Smad7 in psoriasis vulgaris patients: a clinical and immunohistochemical study. *J Cosmet Dermatol*. 2020;19(12):3395-3402. https://doi.org/10.1111/jocd.13425. Epub 2020 Apr 19 PMID: 32307790.
31. Meneguin S, de Godoy NA, Pollo CF, Miot HA, de Oliveira C. Quality of life of patients living with psoriasis: a qualitative study. *BMC Dermatol*. 2020;20:22.
32. Ali YH. Laser-assisted lipolysis burn safety: proposed detailed parameters with assessment of their efficacy and safety. *Plast Reconstr Surg Glob Open*. 2018;6(10):e1934. https://doi.org/10.1097/GOX.0000000000001934. Published 2018 Oct 3.

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