The Egyptian Journal of Hospital Medicine (July 2025) Vol. 100, Page 4454-4463

Evaluation of The Efficacy and Safety of Topical Cyclosporine 2% Gel versus Topical Liposomal Formulation of Cyclosporine 2% in Mild to Moderate Stable Plaque Psoriasis: Clinical, Dermoscopic and Histopathologic Study

Amina Khedr Abdelaziz*, Maha A. Elgayar, Amany Awad
Department of Dermatology, Andrology & STDs, Faculty of Medicine, Mansoura University, Egypt
***Corresponding Author**: Amina Khedr Abdelaziz, **Mobile**: (+20) 10 92513475,
Email: amona.khedr@gmail.com

ABSTRACT

Background: Psoriasis vulgaris (PV) is a chronic inflammatory skin disease with an immunological basis, characterized by alternating phases of flare-ups and remission. Oral cyclosporine is commonly used in the management of severe recalcitrant plaque psoriasis (Ps).

Objectives: This study aimed to assess the efficacy and safety of topical cyclosporine 2% gel versus topical cyclosporine 2% in liposomal formulation in the management of chronic stable mild to moderate plaque Ps.

Patients and Methods: The study included 30 patients with chronic stable mild to moderate plaque Ps. Each participant applied topical cyclosporine 2% gel on lesions of the right side of the body and topical cyclosporine 2% liposomal formulation on lesions of the left side once daily for 12 weeks. Lesions were scored according to PASI index and the Erythema, Scaling & Infiltration Score System at baseline, after 1 month, 2 months, and 3 months of treatment.

Results: The present study revealed that Erythema, induration and scales decreased significantly in both groups at 1, 2, and 3 months compared to baseline with a statistically significant improvement in the clinical findings in both groups along the treatment course in both study groups**.** There was statically significant improvement in the dermoscopic findings including red dots, scales and Pink background in both groups during the treatment course in both study groups. The degree of improvement was higher in the cases treated with topical cyclosporine 2% liposomal formulation.

Conclusion: Both preparations resulted in significant clinical and dermoscopic improvement; however, the liposomal formulation demonstrated superior efficacy.

Keyword: Topical Cyclosporine, Liposomal Formulation, Stable Plaque Psoriasis.

INTRODUCTION

Psoriasis (Ps) is a chronic inflammatory disease manifested primarily as skin lesions with a subsequent affection of life quality [1]. Resident KCs and immune cells are responsible for the occurrence and maintenance of Ps' inflammatory condition. Despite the various treatment options proposed in Ps treatment, discovering an adjuvant therapy to aid current ones is still a challenge for clinicians [2]. Cyclosporine-A (Cyc-A) as an immunosuppressant agent selectively suppresses the proliferation of Th cells [3]. Cyc-A has been used as a therapeutic modality to Ps on the other hand, it could cause toxicity and critical adverse events [4]. Topical therapy as the initial therapeutic modality in the management of Ps is a promising plan by delivering medications effectively into the targeted areas, minimizing systemic adverse events of medications and confirming high patient compliance [5]. Topical delivery of Cyc-A across the stratum corneum is affected by its molecular size (1202 Da), and lipophilicity as well as by its cyclic molecular structure [6].

Liposomal carriers are assessed as a method of improving the clinical efficiency of numerous topical agents as Cyc-A secondary to the resemblance of lipid structure of Liposomes to membranes of keratinocytes [7]. The local application of Cyc-A Loaded microemulsion based Carbopol 940 gel was utilized to enhance the permeation and drug retention for the efficient management of Ps [4]. This study aimed to assess aimed to assess the efficacy and safety of topical cyclosporine 2% gel vs. topical cyclosporine 2%in liposomal formulation in the management of chronic stable mild to moderate plaque Ps.

PATIENTS AND METHODS

This prospective, comparative, split-body clinical study included 30 consecutive middle-aged patients with bilaterally symmetrical, chronic, stable plaque psoriasis, attending the Outpatient Clinic of the Department of Dermatology, Andrology, and STDs, Mansoura University Hospitals, Mansoura, Egypt, during the period from October 2023 to October 2024.

The disease was diagnosed clinically and confirmed by dermoscopic examination, characterized by sharply demarcated erythematous scaly plaques persisting for at least two months.

All patients were informed to apply the assigned preparation once daily for 12 weeks cyclosporine 2% gel on lesions on the right side of the body **(Group 1)** and cyclosporine 2% in liposomal formulation on lesions on the left side of the body **(Group 2).**

Inclusion criteria: Adults patients with mild to moderate plaque types of PV comprising less than 10% body surface area and both genders.

Exclusion criteria: Pregnant or breastfeeding females; patients with systemic diseases such as hepatic or renal disease, hypertension, active infection, or malignancy; patients with other dermatological diseases (e.g., atopic dermatitis, vitiligo, systemic lupus erythematosus); patients who received systemic treatment for psoriasis (e.g., methotrexate or cyclosporine) within six months

Received: 02/05/2025
Accepted: 04/07/2025

prior to enrollment; patients who received UVB phototherapy within two months prior to enrollment; heavy smokers; children; patients with hypersensitivity to cyclosporine; and patients with pustular or erythrodermic psoriasis.

All participants were subjected to full history taking, ccomplete physical examination included general examination to exclude any systemic diseases and dermatological examination, comprising skin, hair, and nails to evaluate the clinical form of Ps, distribution and severity and to rule out autoimmune skin disorders. Lesions were scored based on PASI score. The PASI score was utilized to assess the disease and combine the evaluation of the severity of lesions and the area affected into a single score in the range from zero (no disease) to 72 (maximum disease). The body is divided into four areas [head (ten percent of a subject's skin), arms (twenty percent), trunk (thirty percent), and legs (forty percent)]. Each area is scored individually, and then they are combined into the final PASI. The PASI score classifies cases with Ps into mild Ps (PASI ≤10), moderate Ps (PASI more than ten and less than 20), and severe Ps (PASI ≥20) [8]. Each area must be examined individually. The severity is measured by 3 clinical features: erythema (redness), induration (thickness) and desquamation (scale formation). Severity scale is assessed from zero to four [9]. Then, the weight of the corresponding portion is multiplied by the area score for each area, and the total of the three severity parameters is assessed for each area separately.

Erythema, Scaling and Infiltration (ESI) Score System was utilized in which the affected areas were assigned on a score from zero to four, as follows; none (zero), mild (one), moderate (two), severe (three), or very severe (four). Evaluation of the percentage area affected in each regions was assessed as nil (score zero), < 10 % (score I), 10% - 29% (score II), 30% - 49 % (score III), 50% - 69% (score IV), 70% - < 89% (score V) or 90% - < 100% (score VI) [10].

Dermoscopic examination

Dermoscopy was done for all patients by using Dermlite II PRO.HR (three Gen, Unites States of America) that was palm sized, with high light output, a 25mm 10X lens, camera adaptability, and lithium-ion battery. Assessment was done according to features of vessels (red dots), scales (No scales, Diffuse, Patchy / clustered or Sporadic) and pink background (No pink background, Dark and Light).

Application of drugs

Both cyclosporine 2% gel and cyclosporine 2% liposome were applied only to the psoriatic lesion, and the patients were informed to recognize the signs of dermatitis, irritation or any other undesirable side effects. Sandimmune Neoral 100 mg ® oral capsules contained 0.9 ml of clear faintly yellow solution of micro-emulsion preconcentrate comprising 100mg cyclosporine as an active ingredient. Additional materials were obtained from Al shobrawishy company. Gel and liposome were prepared at the Pharmacology Lab, Faculty of Medicine Mansoura University and were preserved in closed aluminum tubes.

Preparation of cyclosporine 2% gel

Gel base was prepared using Sodium carboxymethyl cellulose (Na CMC), glycerin, and propylene glycol in distilled water. Gel preparation was mixed while stirring with contents of 5 capsules cyclosporine 100mg then was incorporated the base with five min continuous triturating and stirring to obtain homogeneous clear drug-gel solution.[11]

Preparation of cyclosporine 2% liposome

Using a typical thin-film approach, cyclosporine-loaded liposomes were formed by optimally entrapping the medication, that is, in multilamellar liposomes made of high-purity phosphatidylcholine and other suitable liposomal contents. The formulation included submicron-sized (mean size of d50950nm) cyclosporine-loaded liposomes with an ideal drug payload of 142 μg/mg and a drug entrapment percentage of 97.4%, which were distributed in a hydrophilic carbopol 940 gel to offer the best rheological characteristics [7].

Skin specimens

Skin specimens were obtained from the two lesions of two haphazardly chosen cases of each group under local anesthesia with 1% lidocain pre and post twelve weeks of treatment, then stained with H&E.

Follow up

Each patient was assessed regarding the dermoscopic features pre- and post-treatment. Also, the follow up of PASI score and ESI score was performed pre-treatment, at one month, at two months and at three months of treatment.

***Ethical Consideration*:**

This study was ethically approved by Mansoura University's Research Ethics Committee (MS.- IRB #23.02.2309). Written informed consent was obtained from all participants. The study protocol conformed to the Helsinki Declaration, the ethical norm of the World Medical Association for human subjects.

Statistical analysis

Results were analysed by using SPSS 22.0, IBM/SPSS Inc., Chicago, IL). Qualitative data was presented by frequency tables (Number and percentages). For analytical or inferential statistics Chi-Square test, Fisher's exact test, Monte-carlo test, student T, Mann Whitney Test (U test), Paired samples t-Test, Wilcoxon Test, McNamar's test and Marginal homogeneity test were used. *P*-values < 0.05 are .significant

RESULTS

The current study included 30 cases with localized plaque psoriasis having symmetrical lesions affecting both legs and arms. The mean age of the cases was 49.7 ± 13.11 years. There were 12 males (40%) and 18

females (60%). There were 8 smokers (26.7%) and 14 cases with high BMI) (table 1(

Table (1): Demographic and clinical data in the cases of the study

Variables		**Study cases (N = 30)**	
Age (Years)	Mean ± SD	49.7 ± 13.11	
		N	**%**
Sex			
Male		12	40
Female		18	60
Smoking			
No		22	73.3
Yes		8	26.7
BMI (kg/m^2)			
Normal		16	53.3
High		14	46.7

Table **(2)** demonstrates statistically significant improvements in all evaluated parameters over the treatment periodPsin group 1. Erythema demonstrated significant improvement at 1-, 2-, and 3-months post-treatment compared to pre-treatment, as well as between each consecutive time point (1 vs. two months, 1 vs. three months, and 2 vs. three months).

Induration was associated with a significant improvement at 2 and three months compared to basal level, and between 1 and two months, as well as 1 and three months. Scaling significantly improved at 2 and three months compared to pre-treatment, between 1 and two months, and 1 and three months.

ESI (Erythema, Scaling, Induration composite index) significantly decreased at all post-treatment time points (1, 2, and three months) compared to pre-treatment and also demonstrated significant decreases between each month.

PASI score demonstrated a statistically significant decrease at three months post-treatment compared to baseline. These findings collectively indicate a progressive and consistent improvement in clinical symptoms over the 3-month treatment period.

Table (2): Analysis of the clinical findings in the cases of Group 1 (Topical Cyclosporine 2% Gel) along the duration of follow-up

Variables	**Pre-treatment**		**At one month**		**At two months**		**At three months**		**Test of sig.**
	N	%	N	%	N	%	N	%	
Erythema									
+1	0	0	3	10	16	53.3	24	80	P1=0.010*,
+2	4	13.3	15	50	14	46.7	6	20	P2<0.001*
+3	16	53.3	12	40	0	0	0	0	P3<0.001*,
+4	10	33.3	0	0	0	0	0	0	P4=0.009*
									P5<0.001*,
									P6=0.024*
Induration									
0	1	3.3	3	10	17	56.7	21	70	P1=0.109,
+1	6	20	15	50	12	40	9	30	P2<0.001*
+2	14	46.7	10	33.3	1	3.3	0	0	P3<0.001*
+3	7	23.3	2	6.7	0	0	0	0	P4=0.006*
+4	2	6.7	0	0	0	0	0	0	P5=0.001*
									P6=0.092
Scales									
0	0	0	1	3.3	9	30	10	33.3	P1=0.068,
+1	1	3.3	8	26.7	14	46.7	17	56.7	P2<0.001*
+2	9	30	15	50	7	23.3	3	10	P3<0.001*
+3	14	46.7	6	20	0	0	0	0	P4=0.038*
+4	6	20	0	0	0	0	0	0	P5=0.005*
									P6=0.138
ESI	8	(4–12)	5.5	(2–9)	2.5	(1–6)	2	(1–5)	P1<0.001*
									P2<0.001*
									P3<0.001*
									P4<0.001*
									P5<0.001*
									P6=0.010*
PASI	2.2	(1–4.8)	—	—	—	—	0.7	(0.2–2.2)	P3<0.001*

P1: Significance between pre- and one Mo post-treatment, P2: Significance between pre- and two Mo post-treatment, P3: Significance between pre- and three Mo post-treatment, P4: Significance between one month and two Mo post-treatment, P5: Significance between one Mo and three Mo post-treatment, P6: Significance between two Mo and three Mo post-treatment,

*: Statistically significant ($p < 0.05$).

Table **(3)** shows significant improvements in all clinical parameters over the course of treatment in group 2. Erythema significantly improved at 1-, 2-, and 3 months post-treatment compared to pre-treatment, as well as between 1 and two months, and 1 and three months. Induration demonstrated significant improvement at 2 and three months compared to baseline, and between 1 and two months, and 1 and three months. Scaling significantly improved at 1-, 2-, and 3-months post-treatment compared to baseline, with additional improvements between all consecutive time points (1 vs. two months, 1 vs. three months, and 2 vs. three months). ESI significantly diminished at all post-treatment time points compared to pre-treatment and also demonstrated significant reductions between each month. PASI score significantly diminished at three months post-treatment compared with baseline. In general, the results demonstrate a consistent and significant improvement in erythema, induration, scaling, ESI, and PASI scores throughout the 3-month treatment period.

Table (3): Analysis of the clinical findings in the cases of Group 2 along the duration of follow up

Variables	**Pre-treatment**		**At one month**		**At two months**		**At three months**		**Test of sig.**
	N	**%**	**N**	**%**	**N**	**%**	**N**	**%**	
Erythema									
0	0	0	0	0	4	13.3	6	20	P1=0.001*
+1	0	0	5	16.7	18	60	21	70	P2<0.001*
+2	4	13.3	17	56.7	8	26.7	3	10	P3<0.001*
+3	16	53.3	8	26.7	0	0	0	0	P4<0.001*
+4	10	33.3	0	0	0	0	0	0	P5<0.001*
									P6=0.068
Induration									
0	1	3.3	4	13.3	21	70	28	93.3	P1=0.075
+1	6	20	15	50	9	30	2	6.7	P2<0.001*
+2	14	46.7	11	36.7	0	0	0	0	P3<0.001*
+3	7	23.3	0	0	0	0	0	0	P4<0.001*
+4	2	6.7	0	0	0	0	0	0	P5<0.001*
									P6=0.012
Scales									
0	0	0	1	3.3	12	40	21	70	P1=0.029*
+1	1	3.3	8	26.7	17	56.7	8	26.7	P2<0.001*
+2	9	30	21	70	1	3.3	1	3.3	P3<0.001*
+3	14	46.7	0	0	0	0	0	0	P4=0.001*
+4	6	20	0	0	0	0	0	0	P5<0.001*
									P6=0.015*
ESI (Median, Range)	8 (4–12)		5 (2–7)		2 (0–4)		1 (0–4)		P1<0.001* P2<0.001* P3<0.001* P4<0.001* P5<0.001* P6=0.006*
PASI (Median, Range)	2.2 (1–4.8)						0.4 (0–1.6)		P3<0.001*

P1: Significance between pre- and one Mo post-treatment, P2: Significance between pre- and two Mo post-treatment, P3: Significance between pre- and three Mo post-treatment, P4: Significance between one Mo and two Mo post-treatment, P5: Significance between one Mo and three Mo post-treatment, P6: Significance between two Mo and three Mo post-treatment, ***: Statistically significant (p< 0.05).**

Table **(4)** shows that the dermoscopic signs were comparable between both groups pre-treatment without a statistically significant difference between both groups. However, post-treatment, there was a statistically significant improvement in group 2 as compared to group.

Table (4): Comparison of the dermoscopic findings in the two studied groups along pre- and post-treatment

Variables	Group 1 Before		Group 1 After		Group 2 Before		Group 2 After		P value
	N	%	N	%	N	%	N	%	
Red dots									
Absent	0	0	3	10	0	0	11	36.7	P1 = 1 P2 = 0.015* P3 = 0.176 P4 = 0.001*
Present	30	100	27	90	30	100	19	63.3	
Scales									
No scales	0	0	9	30	0	0	21	70	P1 = 0.889 P2 = 0.006* P3 = 0.005* P4 < 0.001*
Diffuse	15	50	0	0	14	46.7	0	0	
Patchy / clustered	13	43.3	2	6.7	13	43.3	0	0	
Sporadic	2	6.7	19	63.3	3	10	9	30	
Pink background									
No pink background	0	0	1	3.3	0	0	9	30	P1 = 1 P2 = 0.006* P3 < 0.001* P4 < 0.001*
Dark	28	93.3	0	0	28	93.3	0	0	
Light	2	6.7	29	96.7	2	6.7	21	70	

P1= Comparison between both groups pre-treatment, P2= Comparison between both groups post-treatment, P3 = Comparison between pre- and post-treatment in group A, P4 = Comparison between pre- and post-treatment in group B, *: Statistically significant ($p< 0.05$).

Table **(5)** shows that there was no statistically significant difference between group 1 and group 2 regarding the degree of improvement of ESI post-treatment at one month and at two months. However, at three months, the degree of improvement was significantly higher in group 2 ($p = 0.001$). Percent of reduction was significantly higher in group 2.

Table **(6)** shows that post-treatment; the PASI score was significantly lower in the cases of group 2. Percent of reduction was significantly higher in group 2.

Table **(7)** shows that there was a statistically significant improvement in post-treatment as compared to pre-treatment in both groups. There was a statistically significant better improvement in group 2 as compared to group 1.

Table (5): Comparison of the clinical findings (ESI) in the two studied groups along the duration of follow up

Variables	Pre-treatment (N=30)		At one month (N=30)		At two months (N=30)		At three months (N=30)		Percent of reduction	Test of sig.
	N	%	N	%	N	%	N	%		
Group 1	8	26.7	5.5	18.3	2.5	8.3	2	6.7	72.23 ± 14.15	P1<0.001* P2<0.001* P3<0.001* P4<0.001* P5<0.001* P6=0.010*
Group 2	8	26.7	5	16.7	2	6.7	1	3.3	83.65 ± 15.37	P1<0.001* P2<0.001* P3<0.001* P4<0.001* P5<0.001* P6=0.006*
P	1	–	0.325	–	0.060	–	0.001*	–	0.004*	–

P: Significance between group 1 and group 2

P1: Significance between pre- and one Mo post-treatment, P2: Significance between pre- and two Mo post-treatment

P3: Significance between pre- and three Mo post-treatment, P4: Significance between one Mo and two Mo post-treatment

P5: Significance between one Mo and three Mo post-treatment, P6: Significance between two Mo and three Mo post-treatment

***: Statistically significant ($p< 0.05$).**

Table (6): Comparison of the clinical findings (PASI) in the two studied groups along the duration of follow up

Variables	**Pre-treatment (N=30)**		**Post-treatment (At three months) (N=30)**		**Test of sig.**
	N	**%**	**N**	**%**	
Group 1					
PASI					
Median (range)	2.2 (1 – 4.8)	–	0.7 (0.2 – 2.2)	–	P1 < 0.001*
Group 2					
PASI					
Median (range)	2.2 (1 – 4.8)	–	0.4 (0 – 1.6)	–	P1 < 0.001*
P2 value	1	–	0.003*	–	–
Percent of reduction (%)	69.50	19.22	83.65	15.37	P2 = 0.003*

P1: Significance between pre- and three Mo post-treatment
P 2: Significance between group 1 and group 2
***: Statistically significant (p< 0.05)**

Table (6): The clinical response in Group 1 (Topical Cyclosporine 2% Gel) and Group 2 (Topical Liposomal Formulation of Cyclosporine 2%)

Variables	**Group 1**				**Group 2**				**P value**	**P3 value**
	Pre-treatment (N=30)		At three months (N=30)		Pre-treatment (N=30)		At three months (N=30)			
	N	**%**	**N**	**%**	**N**	**%**	**N**	**%**		
Erythema										
0	0	0	0	0	0	0	6	20	1	<0.001*
+1	0	0	24	80	0	0	21	70		
+2	4	13.3	6	20	4	13.3	3	10		
+3	16	53.3	0	0	16	53.3	0	0		
+4	10	33.3	0	0	10	33.3	0	0		
Induration										
0	1	3.3	21	70	1	3.3	28	93.3	1	<0.001*
+1	6	20	9	30	6	20	2	6.7		
+2	14	46.7	0	0	14	46.7	0	0		
+3	7	23.3	0	0	7	23.3	0	0		
+4	2	6.7	0	0	2	6.7	0	0		
Scales										
0	0	0	10	33.3	0	0	21	70	1	<0.001*
+1	1	3.3	17	56.7	1	3.3	8	26.7		
+2	9	30	3	10	9	30	1	3.3		
+3	14	46.7	0	0	14	46.7	0	0		
+4	6	20	0	0	6	20	0	0		
ESI (Median, Range)	8 (4–12)		2 (1–5)		8 (4–12)		1 (0–4)		1	<0.001*
PASI (Median, Range)	2.2 (1–4.8)		0.7 (0.2–2.2)		2.2 (1–4.8)		0.4 (0–1.6)		1	<0.001*

P: Comparison between pretreatment value in group 1 vs. group 2
P3: Comparison between posttreatment value in group 1 vs. group 2
***: Statistically significant (p< 0.05)**

CASES PRESENTATION

Figures (1–10) revealed clinical and dermoscopic findings pre- and post-treatment for a psoriatic cases.

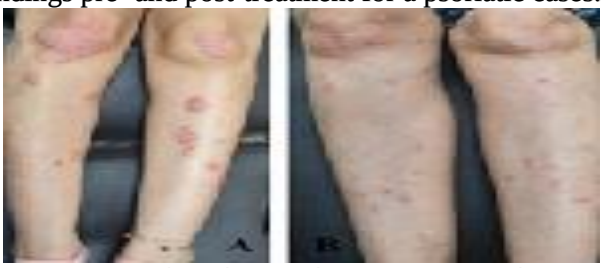

Figure (1): Female patient aged 33 years. Comparison between cyclosporine gel group (right) and cyclosporine liposome group (left) pre- and post-treatment.

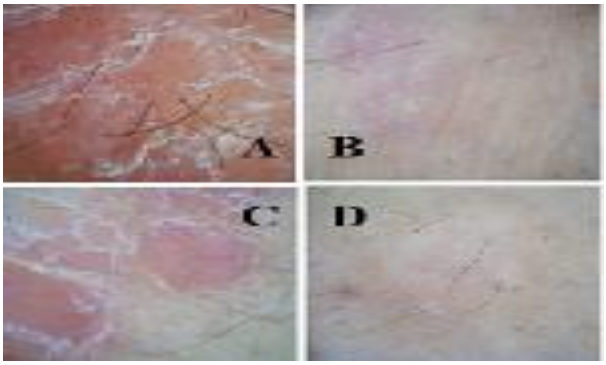

Figure (2): Dermoscopic findings pre- and post-treatment (A, B) cyclosporine gel group, (C, D) cyclosporine liposome group with further improvement in cyclosporine liposome group

Figure (3): Female patient aged 38yrs. Comparison between cyclosporine gel group (right) and cyclosporine liposome group (left) pre- and post-treatment.

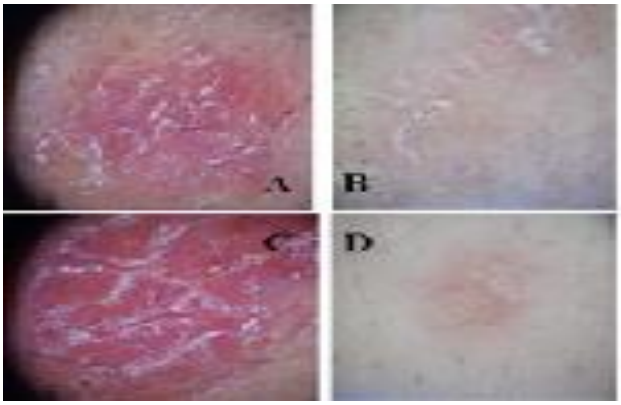

Figure (4): Dermoscopic results pre &post-treatment (A, B) cyclosporine gel group, (C, D) cyclosporine liposome group with further improvement in cyclosporine liposome group.

Figure (5): Female case aged 42yrs. Comparison between cyclosporine gel group (right) and cyclosporine liposome group (left) pre- and post-treatment.

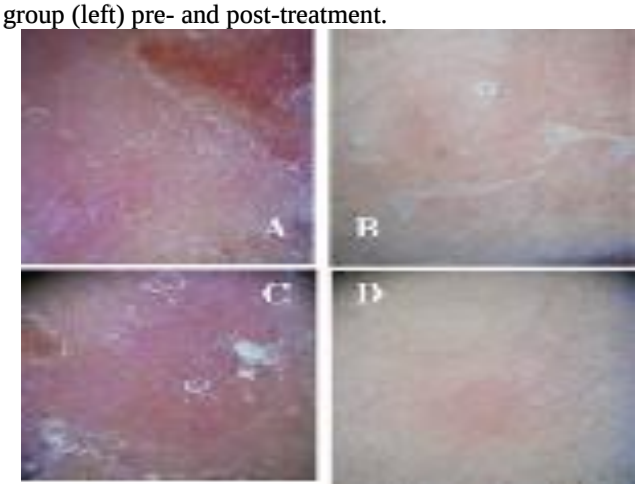

Figure (6): Dermoscopic findings pre- and post-treatment (A,B) cyclosporine gel group, (C,D) cyclosporine liposome group with further improvement in cyclosporine liposome group.

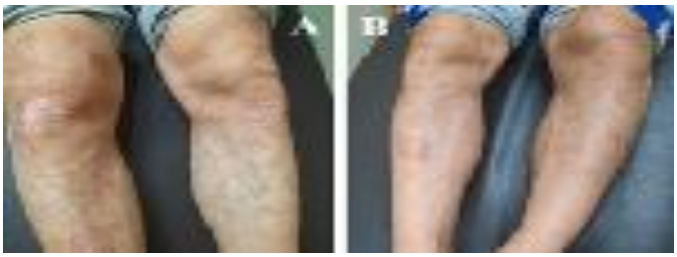

Figure (7): Male case aged 45 yrs. Comparison between cyclosporine gel group (right) and cyclosporine liposome group (left) pre- and post-treatment.

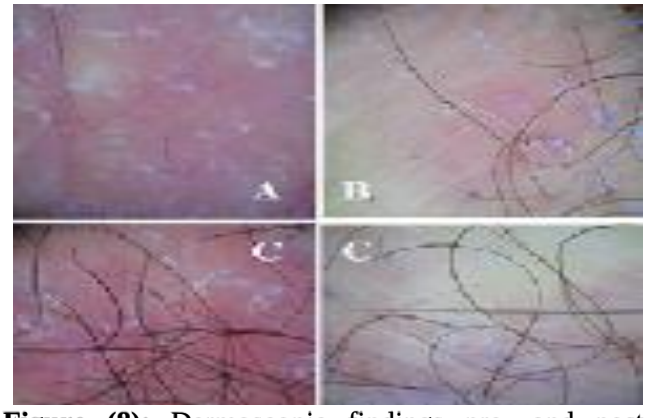

Figure (8): Dermoscopic findings pre- and post-treatment (A, B) cyclosporine gel group, (C, D) cyclosporine liposome group with further improvement in cyclosporine liposome group.

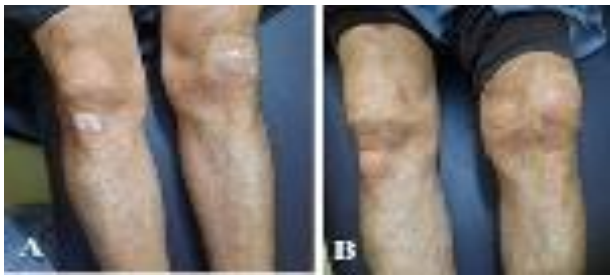

Figure (9): Male case aged 62yrs. Comparison between cyclosporine gel group (right) and cyclosporine liposome group (left) pre- and post-treatment.

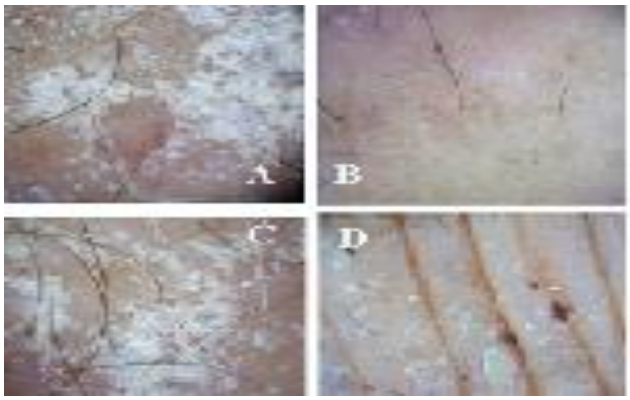

Figure (10): Dermoscopic findings pre- and post-treatment (A,B) cyclosporine gel group, (C,D) cyclosporine liposome group with further improvement in cyclosporine liposome group

DISCUSSION

Psoriasis is a chronic inflammatory skin disease that always needs improving and controlling of physical signs [12]. Oral cyclosporine is required in the management of severe recalcitrant plaque Ps. On the other hand, it is nephrotoxic and has a lot of systemic adverse events. Even though topical delivery of cyclosporine, targeted to the lesional area, could provide considerable benefits, there are no locally-applied formulations approved for dermatologic usage [13]. Due to both physical and chemical properties of thick stratum corneum in psoriasis, Trial topical Formulation suitable for treatment localized plaque psoriasis was mandatory. Scientists are working to enhance the local delivery of cyclosporine by utilizing multiple new drug delivery system [14, 15].

The current study was conducted to assess the efficiency and safety of topical cyclosporine 2% gel versus topical cyclosporine 2%in liposomal formulation in the treatment of chronic stable plaque Ps. The current study included 30 cases with psoriasis. Each patient was instructed to apply the assigned preparation every 24 hours for 12 weeks, Cyclosporine 2% gel on the studied lesions in group (1) and cyclosporine 2% liposome on the studied lesions in group (2).

In the current study, the mean age of the cases in the Ps group was 49.7 ± 13.11 years. In our study, there were 8 active smokers (26.7%), in accordance with **El-Komy *et al.*** [16] who examined 2534 patients with Ps and found that 26.9% were smokers.

The present study revealed that Erythema, induration and scales decreased significantly in both groups at one month, at two months and at three months compared with baseline with a statically significant improvement in the clinical findings (including erythema, induration, scales, ESI and PASI) in both groups along the treatment course in both study groups. The degree of improvement was greater in the cases treated with topical cyclosporine 2% liposomal formulation.

In agreement, **Kumar *et al.*** [7] reported a significant decrease in the Dermatological Sum Score (DSS) following two weeks of use with cyclosporine lipogel, with approximately 83% reduction observed by the eighth week. Notably, full clearance (DSS = zero) was achieved in 41% of the treated sites, highlighting the efficacy of cyclosporine lipogel in managing psoriasis lesions. Additionally, another study on cyclosporine hydrogel ointment for nail psoriasis reported complete response in 24 of 44 nails and partial response in 20 nails, demonstrating the potential of topical cyclosporine formulations in treating localized psoriasis manifestations [17]. Similarly, **Gallo *et al.*** [17] reported favorable outcomes using topical cyclosporine hydrogel in nail psoriasis, suggesting that novel formulations may improve drug penetration and clinical response. To the best of our knowledge this is the first study to use the dermoscope in assessing the response of topical cyclosporine gel and liposome in the management of plaque Ps. In the topical cyclosporin gel group, there was a significant improvement in the scale as detected by dermoscopy, evidenced by improvement of diffuse scales post-treatment as compared to pre-treatment. In addition, there was a statistically significant improvement in the pink background as detected by dermoscopy, detected by improvement of dark pink background post-treatment as compared to pre-treatment.

In the Topical Liposomal Formulation of Cyclosporine 2%, there was a significant improvement in the scale as detected by dermoscopy, evidenced by improvement of diffuse scales post-treatment compared to pre-treatment. Additionally, there was a significant improvement in the pink background as detected by dermoscopy, detected by improvement of dark pink background post-treatment as compared to pre-treatment.

In another study, two groups of cases with chronic plaque Ps were topically treated either with 10% cyclosporine in a jelly base or with 5% cyclosporin in an ointment base under occlusion. Further improvement was seen in lesions treated under occlusion as cyclosporin penetrated more into the lower epidermis and dermis. In contrast to systemic application of cyclosporin, clinical differences between cyclosporine and placebo-treated plaques were minimal increasing the need for optimized formulations [18].

On the contrary, **Bunse *et al.*** [18] observed no significant clinical differences between cyclosporine and placebo when applied topically under occlusion, emphasizing that formulation and delivery systems play a crucial role in therapeutic outcomes. Moreover, **Ogiso**

et al. [19] highlighted that the penetration efficiency of vesicular systems depends on surface charge, with negatively charged liposomes showing superior dermal diffusion compared to positively charged ones, which may explain discrepancies across different studies.

The studies that reported the effect of topical application of systemic drugs in the treatment of Ps are limited. However, **El Gayar *et al.*** [20] performed a study comprised 40 cases with localised plaque Ps informed to apply methotrexate to one side (group A) and CPL to the contralateral side lesions (group B) every 12 hours for 12 weeks. Clinical and dermoscopic assessments pre-, during and post-three months of treatment were conducted. After three months of treatment, group A demonstrated significant improvement in red dots and pink background, and significant improvement in scaling compared to group B.

In general, histopathologic assessment of Ps lesions is an important measure of assessment of response to treatment as shown with assessment of PASI. The histopathology in our study was performed in two cases pre- and post-treatment. The normalization of epidermal hyperplasia, granular layer, orthokeratosis and rete ridges were confirmed post-treatment.

Likewise, **Helmy *et al.*** [13] who revealed that clinical improvement of plaque severity was confirmed by histological examination of specimens taken following treatment with topical cyclosporin, that displayed a reduction in epidermal hyperplasia, and normalisation of dermal papillae lengths. In clinical sitting, they recorded a reduction in plaque elevation, reduction in scale formation and reduction visibility of erythema.

CONCLUSION

This study demonstrates that both topical cyclosporine 2% gel and topical cyclosporine 2% liposomal formulation are effective and safe in the management of chronic stable mild to moderate plaque psoriasis. Both preparations result in significant clinical and dermoscopic improvement; however, the liposomal formulation shows superior efficacy. The results suggested that liposomal cyclosporine could be a promising topical therapeutic option for localized psoriasis, although larger, long-term, and multicenter trials are needed to confirm its role in clinical practice.**Conflict of interest:** None.

Funding: None.

REFERENCES

1. **Bu J, Ding R, Zhou L *et al.*** (**2022**): Epidemiology of psoriasis and comorbid diseases: a narrative review. Front Immunol., 13:880201.
2. **Man A, Orăsan M, Hoteiuc O *et al.*** (**2023**): Inflammation and psoriasis: a comprehensive review. Int J Mol Sci., 24:16095.
3. **Liddicoat A, Lavelle E** (**2019**): Modulation of innate immunity by cyclosporine A. Biochem Pharmacol., 163:472–80.
4. **Pandey S, Tripathi P, Gupta A *et al.*** (**2022**): A comprehensive review on possibilities of treating psoriasis using dermal cyclosporine. Drug Deliv Transl Res., 12:1541–55.
5. **Rapalli V, Singhvi G, Dubey S *et al.*** (**2018**): Emerging landscape in psoriasis management: from topical application to targeting biomolecules. Biomed Pharmacother., 106:707–13.
6. **Carreras J, Tapia-Ramirez W, Sala A *et al.*** (**2020**): Ultraflexible lipid vesicles allow topical absorption of cyclosporin A. Drug Deliv Transl Res., 10:486–97.
7. **Kumar R, Dogra S, Amarji B *et al.*** (**2016**): Efficacy of novel topical liposomal formulation of cyclosporine in mild to moderate stable plaque psoriasis: a randomized clinical trial. JAMA Dermatol., 152:807–15.
8. **Mrowietz U, Kragballe K, Reich K *et al.*** (**2011**): Definition of treatment goals for moderate to severe psoriasis: a European consensus. Arch Dermatol Res., 303:1–10.
9. **Kreft S, Kreft M, Resman A *et al.*** (**2006**): Computer-aided measurement of psoriatic lesion area in a multicenter clinical trial—Comparison to physician's estimations. J Dermatol Sci., 44:21–7.
10. **Ibrahim Abd El Kader A, Ahmed Ibrahim F, Awad Abd El Magied Salime R** (**2024**): Psoriasis Severity and Functional Disabilities among Patients with Psoriasis. Egypt J Health Care, 15:1358–70.
11. **Mittal S, Ali J, Baboota S** (**2021**): Enhanced anti-psoriatic activity of tacrolimus loaded nanoemulsion gel via omega 3-Fatty acid (EPA and DHA) rich oils-fish oil and linseed oil. J Drug Deliv Sci Technol., 63:102458.
12. **Dincer A, Sezer S** (**2022**): Systemic immune inflammation index as a reliable disease activity marker in psoriatic arthritis. J Coll Physicians Surg Pak., 32:6.
13. **Helmy A, El Batreek M, Abdel Fadeel D *et al.*** (**2022**): 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. J Cosmet Dermatol., 21:3362–70.
14. **Torsekar R, Gautam M** (**2017**): Topical therapies in psoriasis. Indian Dermatol Online J., 8:235–45.
15. **Wozel G** (**2008**): Psoriasis treatment in difficult locations: scalp, nails, and intertriginous areas. Clin Dermatol., 26:448–59.
16. **El-Komy M, Mashaly H, Sayed K *et al.*** (**2020**): Clinical and epidemiologic features of psoriasis patients in an Egyptian medical center. JAAD Int., 1:81–90.
17. **Gallo G, Mastorino L, Barilà D *et al.*** (**2022**): Topical cyclosporine hydrogel preparation: A new therapeutic option in the treatment of nail psoriasis. Dermatol Ther., 35:e15917.
18. **Bunse T, Schulze H, Mahrle G** (**1990**): Topical administration of cyclosporin in psoriasis vulgaris. Z Hautkr., 65:538–42.
19. **Ogiso T, Yamaguchi T, Iwaki M *et al.*** (**2001**): Effect of positively and negatively charged liposomes on skin permeation of drugs. J Drug Target, 9:49–59.
20. **El Gayar M, Atwa D, Girgis G *et al.*** (**2022**): Clinical, dermoscopic, and histopathologic evaluation of topical methotrexate 1% hydrogel versus topical Calcipotriol 0.005% cream in the treatment of plaque psoriasis. J Cosmet Dermatol., 21:5779–89.