Al-Azhar Med. J.(Medicine). *Vol. 50(2), April, 2021, 1415 - 1424*
DOI: 10.12816/amj.2021.158621
https://amj.journals.ekb.eg/article_158621.html

EVALUATION OF EFFICACY AND SAFETY OF TOPICAL NICOTINAMIDE FOR TREATMENT OF PSORIASIS VERSUS CALCIPOTRIOL-BETAMETHASONE: COMPARATIVE STUDY

By

Ahmed Saeed Mostafa Anbar, Mohammed Ahmed El-Khalawany and Ahmed Hassan Nouh

Department of Dermatology, Venereology and Andrology, Faculty of Medicine, Al-Azhar University

Corresponding Author: Ahmed Saeed Mostafa Anbar,

Mobile: +201024274795, **E-mail:** anbarman2020@gmail.com

ABSTRACT

Background: Psoriasis is a chronic skin disorder typically characterized by symmetrical erythematous papules and plaques with a silver scale.

Objective: To compare the efficacy and safety of topical nicotinamide for the treatment of mild to moderate psoriasis in Interventional Clinical Trial study compared with calcipotriol-betamethasone.

Patients and methods: Our study was carried out on sixty patients from November 2019 to March 2020, complaining of psoriasis thirty patients treated by topical nicotinamide 4% weekly and thirty patients treated by topical calcipotriol-betamethasone weekly. Patients were selected from out-patient clinic of Dermatology, Venereology and Andrology Department of Al-Azhar University Hospitals.

Results: The present study using topical nicotinamide 4% weekly versus calcipotriol –betamethasone weekly showed lesions on both sides were similar regarding baseline Psoriasis Area and Severity Index (PASI) score ($P = 0.148$), while at 1 month and 3 months after therapy, PASI scores were significantly lower with calcipotriol betamethasone in the second group as compared with nicotinamide alone in first group ($P < 0.001$). At the end of the trial, PASI scores were reduced by 17.9± 7.8 points before treatment to 12.2± 5.08 after 12 weeks with nicotinamide as compared to 16.2 ± 5.5 before treatment to 9.1± 3.2 points with calcipotriol betamethasone ($P < 0.001$).

Conclusion: Nicotinamide can be used for topical psoriasis treatment and may be a good adjuvant to be added to the treatment regimens of psoriasis and it was less effective than calcipotriol betamethasone regarding clinical response and patient's satisfaction.

Keywords: Nicotinamide 4%, Calcipotriol-betamethasone, Psoriasis.

INTRODUCTION

Psoriasis is a chronic proliferative and inflammatory condition of the skin. It is characterized by erythematous plaques covered with silvery scales particularly over the extensor surfaces, scalp, and lumbosacral region *(Elman et al., 2018)*.

The scalp, tips of fingers and toes, palms of the hands, soles of the feet, under the breasts and genital areas, elbows, knees and lower back are most commonly affected sites *(Kuchekar et al., 2011)*.

Clinical presentation is widely variable; some patients may have minimal plaques confined to a small amount of skin surface area and others may have nearly the entire cutaneous surface covered with psoriatic lesions *(Nguyen et al., 2019)*.

The cause of psoriasis is not fully understood, but it is believed to have a genetic component and local psoriatic changes can be triggered by multiple factors that cause insult to the skin *(Parisi et al., 2013)*.

Various environmental factors have been suggested as aggravating to psoriasis, including stress, Certain drugs like chloroquine, lithium, beta-blockers, steroids, and NSAIDs can worsen psoriasis. Generally, summer improves psoriasis while winter aggravates it. Apart from above factors infections, psychological stress, alcohol, smoking, obesity, and hypocalcemia are other triggering factors for psoriasis *(Nguyen et al., 2019)*.

Nicotinamide (niacinamide) is the water-soluble, amide isotype of vitamin B3; niacin (nicotinic acid) is the corresponding acid isotype. Niacinamide an amide of vitamin B3 (niacin) is a hydrophilic endogenous substance. Its effects after epicutaneous application have long been described in the literature *(Chen and Damian, 2014)*.

Given a sufficient bioavailability, niacinamide has antipruritic, antimicrobial, vasoactive, photo-protective, sebostatic and lightening effects depending on its concentration. Within a complex metabolic system niacinamide controls the NFκB-mediated transcription of signalling molecules by inhibiting the nuclear poly (ADP-ribose) polymerase-1 (PARP-1). Niacinamide is a well-tolerated and safe substance often used in cosmetics *(Rovito and Oblong, 2013)*.

Nicotinamide is an inhibitor of poly (ADP-ribose) polymerase-1 (PARP-1) that, through enhancement of nuclear kappa B-mediated transcription, plays a pivotal role in the expression of inflammatory cytokines, chemokines, adhesion molecules, and inflammatory mediators *(Drago et al., 2016)*.

Through interaction with CD38 and inhibition of IL-1, IL-12, and TNF-alpha production, nicotinamide produces a mild TH2 bias. Nicotinamide is a potent phosphodiesterase inhibitor and suppresses neutrophil chemotaxis and mast cell histamine release. It inhibits nitric oxide synthase mRNA induction and suppresses antigen-induced lymphocyte transformation *(Park et al., 2010)*. Nicotinamide increases the biosynthesis of ceramides, which upon degradation produce sphingosine. Sphingosine inhibits protein kinase C (PKC) and decreases basal cell proliferation dependent on PKC *(Morganti et al., 2011)*.

Current treatment strategies of psoriasis are not completely satisfactorily. By inhibiting inflammatory cytokines, nicotinamide may enhance the effects of current topical treatments. Preliminary studies have shown that nicotinamide, which is a vitamin B derivative, is effective in the treatment of psoriasis *(Levine et al., 2010)*.

The aim of this work was to compare the efficacy and safety of topical nicotinamide 4% versus calcipotriol-

betamethasone in the treatment of psoriasis.

PATIENTS AND METHODS

This study was carried out on a total of 60 patients with psoriasis from November 2019 to March 2020. The patients were diagnosed by typical clinical and dermoscopic findings. The patients were able to read and give consents. Patients were selected from out-patient clinic of Dermatology, Venereology and Andrology Department of Al-Azhar University Hospitals.

All patients were subjected to complete medical history, dermatological examination and documented digital photography.

Exclusion criteria:

1. Age below 18 years.
2. Those that used any medication or niacin and multi-vitamins two weeks, or anti-psoriatic systemic drugs or beta-blockers one month prior to the study
3. Patients who>15% of body surface area.
4. Pregnant women.
5. Those with the history of renal, hematologic, liver and major psychiatric diseases.
6. Those with only nail, flexural, palmoplantar, or pustular psoriasis.

The patients were divided into two equal groups (30) patients in each group. Group I was treated with nicotinamide (4%) and Group II with calcipotriol twice daily for 12 weeks. After the first, second and third months of therapy, psoriasis severity was evaluated using the modified psoriasis area and severity index (PASI). Patient's satisfaction was evaluated at the end of the trial using a 10-point rating scale according to dermatology life quality index (DLQI). Serial photographs and dermoscopic examination every month were followed for all patients.

Devices used were:

1. Dermoscope Gen Derma Light 4.
2. Nikon D5300 with Nikkor lens (18-55nm.

Statistical analysis:

Results of the present study were statistically analyzed using SPSS 25 (IBM, USA). Data were represented as median, mean and SD or number and percentage. Numerical data were compared using Mann- Whitney U test while categorical data were compared using Fisher exact test or Chi-square test as appropriate. ROC curve was used to evaluate the performance of different tests differentiate between certain groups. P value < 0.050 was considered significant.

RESULTS

The present study included 60 psoriatic patients divided into two groups.

Regarding demographic data, there was no statistically significant difference between both groups regarding age, sex, duration of lesions and previous treatments.

The patients group included 16males (53%) and 14 females (43%). Their ages range from 18 to 66 years (Mean age ±SD 41.9 ± 16.01). Duration of the disease ranged from 1 year to 17 years (Mean ±SD 8.7 ± 6.5).

As regard the severity of psoriasis, PASI score ranged from 3.6 to 42.5 (Mean ±SD 11.1 ± 7.7).

During the study period, we evaluated 60 patients divided into two groups, from which 7 patients did not match the inclusion criteria and 4 were not willing to participate. Also, during the study period, 5 patients in first group treated with nicotinamide discontinued the trial due to dissatisfaction with therapy. And they were replaced by other patients who are willing to complete the study.

Thus, a total number of 60 patients (16 males), (14 females) in the first group and (17males), (13females) in the second group with mean age of 36.5 ± 8.5 (22-56) years completed the trial. The PASI score of each side of the cases at three measurements were recorded. Analyses showed that lesions on both sides were similar regarding baseline PASI score (P = 0.148), while at 1 month and 3 months after therapy, PASI scores were significantly lower with calcipotriol betamethasone in group one as compared with nicotinamide alone (P < 0.001). At the end of the trial, PASI scores were reduced by 17.9± 7.8 points before treatment to 12.2± 5.08 after 12 weeks with nicotinamide as compared to 16.2 ± 5.5 before treatment to 9.1± 3.2 points with calcipotriol-betamethasone (P < 0.001- **Table 1**).

There was no statistically significant difference (p-value > 0.05) between studied groups as regard sex, age and duration of lesions **(Table1)**.

Table (1): Comparison between studied groups as regard demographic data

Demographic data \ Groups		Group I (N = 30)		Group II (N = 30)		P-value
Sex	**Male**	16	53.3%	17	56.7%	0.795
	Female	14	46.7%	13	43.3%	
Age (years)	**Mean**	41.7		42.3		0.857
	±SD	± 15.5		± 11.4		
Duration (years)	**Mean ±SD**	4.3 ± 2.6		3.4 ± 2.8		0.084
	Median	4		3		

MW: Mann-Whitney Test.

There were statistically significant differences (p-value < 0.05) between PASI score (before & after) in group I and highly statistically significant differences (p-value < 0.001) between PASI score (before & after) in group II **(Table2)**.

Table (2): Comparison of PASI score (before & after) in group I & group II

Groups \ PASI Score		Before (N = 30)	After (N = 30)	P-value
Group I	Mean ±SD	14.9 ± 7.8	11.1 ± 6.7	0.023
	Median	14.2	9.75	
Group II	Mean ±SD	16.2 ± 5.05	9.01 ± 3.2	< 0.001
	Median	16.5	8.6	

MW: Mann-Whitney Test.

There was a statistically significant difference (p-value < 0.001) between studied groups as regard DLQI score **(Table 3)**.

Table (3): Comparison between studied groups as regard DLQI score

Parameters \ Groups		Group I (N = 30)		Group II (N = 30)		P-value
DLQI score	Mean ±SD	7.6 ± 3.8		16.7 ± 4.5		< 0.001
	Median	7		18		
DLQI score categories	No effect	3	10%	0	0%	< 0.001
	Small effect	5	16.7%	0	0%	
	Moderate effect	15	50%	5	16.7%	
	Very large effect	7	23.3%	25	83.3%	

MW: Mann-Whitney Test, X2: Fisher's exact test.

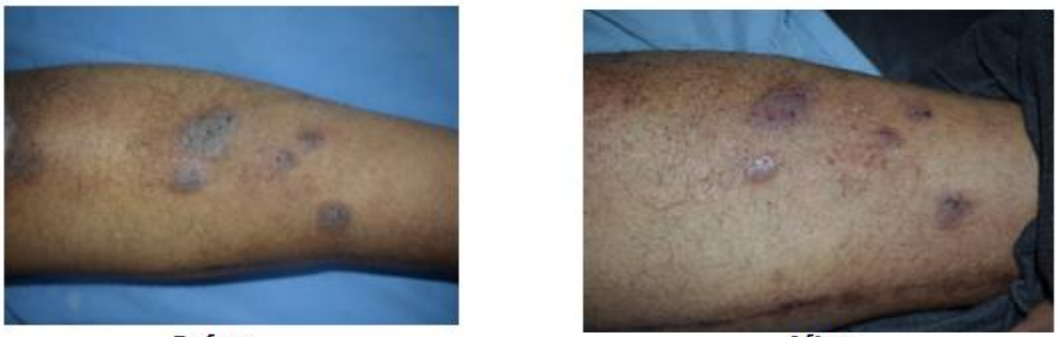

Fig (1): A 35 years old male with psoriasis before and after treatment with topical nicotinamide.

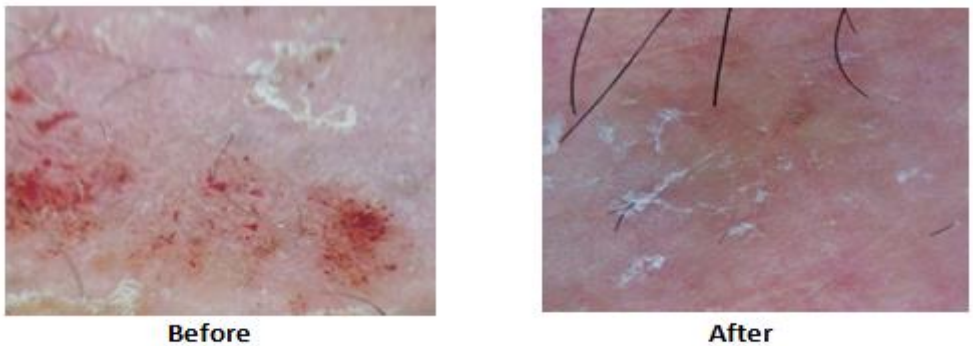

Fig (2): Dermoscopic pictures before and after treatment with topical nicotinamide.

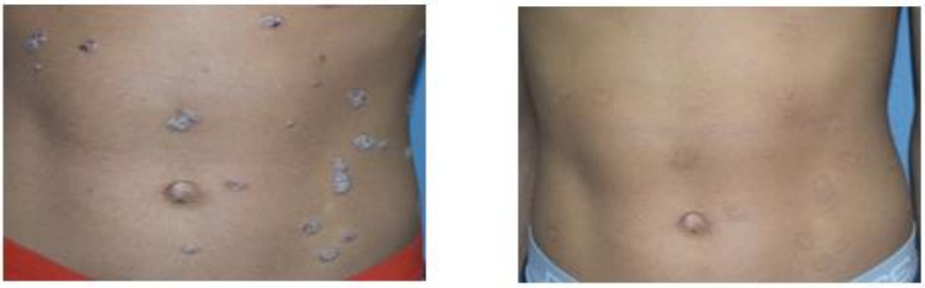

Fig (3): A 18 years old male with psoriasis before and after treatment with topical calcipotriol-betamethasone.

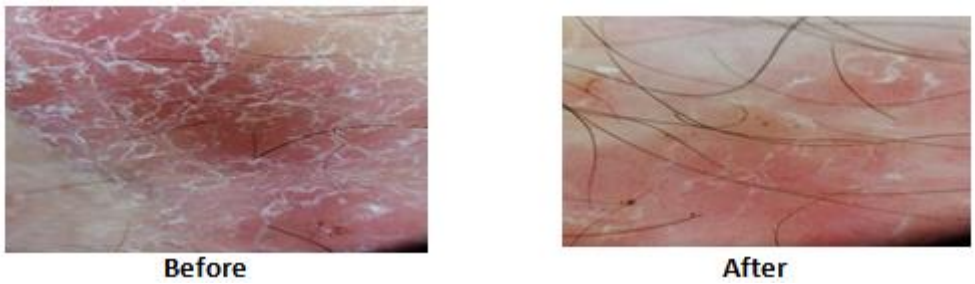

Fig (4): Dermoscopic pictures before and after treatment with topical calcipotriol-betamethasone.

DISCUSSION

Current therapies of psoriasis are not completely satisfactorily. Topical steroids are the most frequently used treatments for psoriasis; however, because of various unwanted effects of long-term use of corticosteroids, such as infections, drug dependency, and skin breakdown, asserting to improve more corticosteroid-sparing regimens has been under attention for the treatment of psoriasis. These agents include vitamin D-analogs (e.g., calcipotriol and tacalcitol), vitamin A-analog (e.g., tazarotene), tars, and topical immunosuppressants as single agents or in combination with other treatments *(Bailey et al., 2012)*.

Our study was carried out on sixty patients complaining of psoriasis, thirty patients treated by topical nicotinamide (4%) weekly and thirty patients treated by calcipotriol-betamethasone weekly, all patients completed the study. Patients were more satisfied regarding improvement of lesions for which they had used calcipotriol-betamethasone as compared with nicotinamide.

Our data showed that calcipotriol-betamethasone combination of is more effective than nicotinamide in reducing the patient's symptoms and also regarding treatment satisfaction in psoriasis while exerting no specific or severe adverse effects.

In literature, there are no studies about using topical nicotinamide alone in treatment of psoriasis.

Our study was the first clinical trial to use topical nicotinamide alone and compare its results to calcipotriol-betamethasone.

Because of the lack of data, we investigated the beneficial effects of adding nicotinamide to for patients with mild to moderate psoriasis in a relatively large sample of patients to compare it with calcipotriol-betamethasone.

In agreement with this study, *Alvarez et al. (2011)* showed that calcipotriol is safe for long-term use in psoriasis. It can be used in combination with corticosteroids or alone. Studies showed a marked reduction of psoriatic plaques in the treatment with calcipotriol and corticosteroids including betamethasone. Also, these combinations were well tolerated by patients.

In another double-blinded trial, *Levine et al. (2010)* divided patients with psoriasis into groups of calcipotriene 0.005% alone, nicotinamide 1.4% alone, and calcipotriene 0.005% plus nicotinamide 0.05%, 0.1%, 0.7%, and 1.4%. Trial was continued for 12 weeks and authors found that half of the patients in nicotinamide + calcipotriene group achieved a good response to the treatment as compared with 18.8% with placebo, 25% with nicotinamide alone, and 31.5% with calcipotriene alone, which was in partial agreement with this study, but with better results which may be due to using a combination of nicotinamide + calcipotriene.

Similarly, a study done by *Siadat et al. (2013)* who showed that the effect of topical nicotinamide in combination with calcipotriol for the treatment of mild to moderate psoriasis and the study showed Nicotinamide can enhance the efficacy of calcipotriol when used in combination for topical psoriasis treatment, and it may be a good adjuvant to the current treatment regimens of psoriasis.

There were some limitations for our study. The modified PASI score that we used for the assessment of psoriasis has the limitation of inter-observer variations. Also, the duration of 12 weeks of therapy was not sufficient to demonstrate the complete effects and side effects of using nicotinamide as a long-term treatment for psoriasis.

CONCLUSION

Nicotinamide can be used for psoriasis treatment with limited effect and may be a good adjuvant to be added to other treatment regimens of psoriasis. Further trials with long-term follow-up are required to confirm these results and also to evaluate possible adverse effects with long-term use of nicotinamide.

Conflicts of interest: no conflicts of interest were encountered.

Acknowledgement: The authors are grateful for the patients without whom this study would not have been done.

REFERENCES

1. **Alvarez AC, Rodríguez-Nevado I and De Argila D (2011):** Recalcitrant pustular psoriasis successfully treated with adalimumab. Pediatr Dermatol., 28: 195–197.
2. **Bailey EE, Ference EH, Alikhan A, Hession MT and Armstrong AW (2012):** Combination treatments for psoriasis: A systematic review and meta-analysis. Arch Dermatol., 148:511–22.
3. **Chen AC and Damian DL (2014):** Nicotinamide and the skin. Australas J Dermatol., 55: 169– 75.
4. **Drago F, Ciccarese G and Parodi (2016): Nicotinamide for skin-cancer chemoprevention. N Engl J Med., 374: 789–90.**

5. **Elman SA, Weinblatt M and Merola JF (2018):** Targeted therapies for psoriatic arthritis: an update for the dermatologist. Semin Cutan Med Surg., 37(3):173-181.
6. **Kuchekar AB, Pujari RR, Kuchekar SB, Dhole SN and Mule PM (2011):** Psoriasis: A comprehensive review. Int. J. of Pharm. & Life Sci., 2:857-877.
7. **Levine D, Even-Chen Z, Lipets I, Pritulo OA, Svyatenko TV and Andrashko Y (2010):** Pilot, multicenter, double-blind, randomized placebo-controlled bilateral comparative study of a combination of calcipotriene and nicotinamide for the treatment of psoriasis. J Am Acad Dermatol., 63:775–81.
8. **Morganti P, Berardesca E, Guarneri B, Guarneri F, Fabrizi G and Palombo P (2011):** Topical clindamycin 1% vs. linoleic acid-rich phosphatidylcholine and nicotinamide 4% in the treatment of acne: A multicentre-randomized trial. Int J CosmetSci., 33:467–76.
9. **Nguyen CT, Bloch Y, Składanowska K, Savvides SN and Adamopoulos IE (2019):** Pathophysiology and inhibition of IL-23 signaling in psoriatic arthritis: A molecular insight. Clin. Immunol., 206:15-22.
10. **Parisi R, Symmons DP, Griffiths CE and Ashcroft DM (2013):** Impact project team Global epidemiology of psoriasis: A systematic review of incidence and prevalence. J. Invest. Dermatol., 133:377–385.
11. Park J, Halliday GM and Surjana D (2010): Nicotinamide prevents ultraviolet radiation-induced cellular energy loss. Photochem Photobiol., 86: 942– 8.
12. **Rovito H and Oblong J (2013):** Nicotinamide preferentially protects glycolysis in dermal fibroblasts under oxidative stress conditions. Br J Dermatol., 169: 15– 24.
13. **Siadat AH, Iraji F, Khodadadi M and Jary MK (2013):** Topical nicotinamide in combination with calcipotriol for the treatment of mild to moderate psoriasis: A double-blind, randomized, comparative study. J Res Med Sci., 18(2): 115–117.

تقييم فعالية وأمان النيكوتيناميد الموضعي في مرضى الصدفية مقارنة بالكالسيبوتريول بيتاميثازون (دراسة مقارنة)

أحمد سعيد مصطفي عنبر، محمد أحمد الخلواني، أحمد حسن نوح

قسم الأمراض الجلدية والتناسلية وأمراض الذكورة، كلية الطب، جامعة الأزهر

خلفيـــة البحـــث: يُعـــد مـــرض الصـــدفية مرضًـــا جلـــديًا يحـــدث عنـــدما تتســـارع دورة حيـــاة خلايـــا الجلـــد. تتســـبب الصـــدفية فيتـــراكم الخلايـــا بســـرعة علـــى ســـطح الجلـــد. وقـــد تجعلـــك خلايـــا الجلـــد الزائـــدة الناتجـــة عـــن القشـــور والبقـــع الحمـــراء تشـــعرأحيانًا بالحكـــة والألـــم. تختلـــف علامـــات وأعـــراض الصـــدفية مـــن شـــخص لآخـــر. وتتضـــمن الأعـــراض والعلامـــات الشـــائعة مـــايلي: بقـــع حمراءعلـــى البشـــرة تغطيهـــا قشـــور فضـــية وســـميكه بقعقشـــرية صـــغيرة (تظهرعـــادة لـــدى الأطفـــال) وبشـــرة جافـــة ومتشـــققة قـــد تنـــزف، الحكـــة أوالحرقان ووجع وأظافرسميكة أومنقرة أومجعدة ومفاصل متورمة ومتيبسة.

ويُعـــد مـــرض الصـــدفية مرضًـــا مزمنًـــا والـــذي غالبًـــا يظهرويختفـــي ويُعـــد الهـــدف الرئيسي من العلاج هومنع نمو خلايا الجلد بشكل سريع.

الهـــدف مـــن البحـــث: تقيـــيم فعاليـــة وســـلامة النيكوتينامیـــد الموضـــعي لعـــلاج مرضـــي الصـــدفية فـــي دراســـة التجـــارب الســـريرية التداخليـــة مقارنـــة مـــع كالســـيبوتريول بيتاميثازون.

طـرق ومـواد البحـث: هـذه الدراسـة هـي التجـارب السـريرية العشـوائية التـي تـم تنفيـذها علـى 60 مـن المرضـى الـذين حضـروا إلـى العيـادة الخارجيـة للأمـراض الجلديـة بمستشـفيات جامعـة الأزهـر فـي الفتـرة مـن نـوفمبر 2019 حتـى مـارس 2020. تـم إخضـاع جميـع المشـاركين أو ذويهـم إلـى: أخـذ التـاريخ الشخصـي والمرضـي كـاملا. فحص جلدي يتضمن أماكن الصدفية. التقاط الصور قبل وبعد العلاج.

تم تقسيم المرضى بالتساوي إلى مجموعتين كل مجموعة تتكون من 30 مريض:

المجموعة الاولي: استخدمت النيكوتينامين الموضعي 4 % **والمجموعة الثانية**: استخدمت الكالسيبوتريول وتم متابعة المرضي أسبوعيا لمدة ثلاثة أشهر وتقييم مستوي فعاليته ودوره في علاج مرض الصدفية.

نتائج البحث: إستخدام الكالسيبوتريول الموضعي أكثر فعالية وأمانا في العلاج مقارنة باستخدم النيكوتينامد الموضعي مع وجود أعراض جانبية أقل.

الاستنتاج: إستخدام الكالسيبوتريول الموضعي أكثر فعالية وأمانا في علاج مرضي الصدفية مقارنة باستخدام النيكوتينامد الموضعي مع وجود أعراض جانبية أقل، مع التوصية بعمل مزيد من الدراسات علي علاج النيكوتينامد الموضعي واستخدامه في مرضي أكثر في دراسات مستقبلية.