A double-blind, randomized controlled trial on the efficacy and safety of 4% niacinamide cream on the treatment of mild to moderate chronic plaque psoriasis at the University of Santo Tomas Hospital Out-Patient Department

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ABSTRACT

Background: Niacinamide is known for its anti-inflammatory effect and skin penetration capability. Currently, limited studies are available on its efficacy on psoriasis.

Objective: This study aimed to determine the efficacy and safety of 4% niacinamide cream on mild to moderate psoriasis.

Methods: 40 patients were randomly allocated to 4% niacinamide cream (N), or 0.1% triamcinolone acetonide cream (TAC) or 4% niacinamide cream and 0.1% triamcinolone acetonide cream (N-TAC) for 10 weeks treatment. A 50% improvement in psoriasis area severity index (PASI50) was considered as the primary endpoint of the study. Secondary outcome measures were physician global assessment (PGA), dermatology life quality index (DLQI), and adverse events. PASI and PGA were assessed biweekly. DLQI was assessed at the start and at the end of the study period.

Results: PASI50 was achieved in 85% of patients in N-TAC, 75% of patients in TAC and 15% of patients in N. There was no statistical significant difference between groups TAC and N-TAC (p=0.645, Fisher's exact test). A higher number of patients in N-TAC (31%) achieved PGA1 score or "almost clear" and reached PASI50 earlier (60% at week 4). A higher improvement in DLQI score was seen in N-TAC; however, mean DLQI improvement did not vary by treatment group (p=0.0770). No adverse event was reported for groups TAC and N-TAC while pruritus and erythema were noted in N.

Conclusion: Monotherapy of 4% niacinamide cream was not effective in the treatment of mild to moderate psoriasis. The combination N-TAC showed a continuous and sustained improvement of lesions compared to monotherapy TAC.

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INTRODUCTION

Psoriasis is a dermatologic condition resulting from an underlying immune system dysregulation and inflammation.[1] Worldwide prevalence of psoriasis is <6% in the adult population.[2] The most common type is chronic plaque psoriasis.[3,4] In the Philippines, a tertiary government hospital reported a prevalence of 2.4%.[5] Moreover, quality of life was found to be lower in patients with psoriasis.[2]

Topical corticosteroids are currently the standard of treatment for mild to moderate psoriasis.[5] However, its prolonged use can result to its known adverse effects such as atrophy, telangiectasia, acneiform eruption and hypopigmentation. In addition, tachyphylaxis and eventual flare-ups have been observed to occur with its use.[1]

Poor drug permeability in thickened psoriatic skin remains to be a challenge for most potential new topical treatments. [6] Niacinamide recently gained popularity in the field of dermatology due to its anti-inflammatory effect as well as its skin penetration capability. [7–9] A study on moderate psoriasis showed that topical low dose 1.4% niacinamide or 0.005% calcipotriene when used alone were inferior to the combination therapy[10], which exhibited an interesting synergistic effect. [10,11] There is still a need to provide mild to moderate psoriasis patients an alternative treatment in order to improve their quality of life while reducing the burden it confers.

This study aimed to determine the efficacy and safety of topical 4% niacinamide cream in the treatment of mild to moderate psoriasis. Specifically, it aimed to compare the effect of 4% niacinamide cream with 0.1% triamcinolone acetonide cream, and with the combination of the two treatments (4% niacinamide cream + 0.1% triamcinolone acetonide cream) in improvement of psoriatic lesions at 2nd, 4th, 6th, 8th and 10th week of follow-up based on the proportion of patients with PASI50 and PGA score of 1 or 'almost clear'. DLQI was assessed at baseline and at the end of the 10-week treatment.

METHODOLOGY

Research Design

The study employed a double-blind, randomized controlled trial with a parallel group design to determine the efficacy and safety of 4% niacinamide cream on the treatment of mild to moderate psoriasis. Patients were randomly allocated into three groups—4% niacinamide cream + placebo, 0.1% triamcinolone acetonide cream + placebo, and 4% niacinamide cream + 0.1% triamcinolone acetonide cream. Patients were followed up every 2 weeks for a period of 10 weeks from the date of study enrollment. Photographs were obtained at baseline and every follow up.

Study Population

Patients who sought treatment for mild to moderate psoriasis at the out patient department of the University of Santo Tomas Hospital (USTH) from August to October 2018.

Inclusion Criteria

Patients aged 18 years old and above diagnosed with mild to moderate chronic plaque-type psoriasis (<10 to <30% body surface area involvement) were included in this study.

Exclusion Criteria

Patients with known hypersensitivity to niacinamide, had lesions on the face, axilla and inguinal area, pregnant and lactating, had present history of immunosuppression, active infection or were mentally disabled and refused or unable to consent were excluded from this study.

Sample Size

PASS 2008 was used to calculate the minimum sample size of the study. A sample of 39 patients with mild to moderate psoriasis achieved 80% power to detect a difference in the proportion of patients who achieved PASI50 at the end of the treatment period. A previous study showed that PASI50 was achieved by 66% of psoriasis patients after treatment with 0.1% triamcinolone acetonide cream12 and it was assumed that 50% of N and 100% of N-TAC patients will achieve PASI50 at the end of the 10-week treatment. Sample size computation for chi square test was used to specify an effect size of 0.5, degree of freedom of 2 and alpha equal to 0.05.

Sampling Methodology

Convenience sampling was employed in the selection of study participants. Each patient diagnosed with psoriasis was screened for eligibility during his or her visit to the USTH outpatient department.

Data Gathering Procedure

Ethical consideration

The study was approved by the USTH Institutional Review Board.

Selection and recruitment process

Recruitment took place in the outpatient department of USTH by a dermatology resident not involved in other study procedures. Eligible patients based on the inclusion and exclusion criteria of the study were referred to the study coordinator to obtain their written consent.

Randomization, allocation concealment, blinding

Prior to the start of the study, an independent researcher not involved in the study generated the allocation schedule. Open Epi random number generator was used in order to generate the list of patient numbers which was assigned to any of the three groups: N, TAC and N-TAC in a ratio of 1:1:1. Simple randomization technique was utilized. The independent researcher prepared sequentially numbered containers of the same size, color, and shape that contained the three medications. The allocation schedule was concealed from study researchers until study termination.

Patients who satisfied the inclusion/exclusion criteria were instructed to withhold medications for psoriasis prior to study inclusion—washout period was 2 weeks for topical corticosteroids and phototherapy and 4 weeks for systemic therapy.[13–15] The coordinator explained the study procedure after which a written consent was obtained to affirm voluntary participation. Patients were assigned a number sequentially according to their study entry by the study coordinator. Socio-demographic and baseline information were recorded using a data collection form. Baseline photographs were also obtained. Both the patient and the outcome assessors were blinded to the treatment allocation throughout the study.

Interventions

The study coordinator gave two cream containers to the patients that corresponded to their study number.

- N: 4% niacinamide cream (A) then placebo (B) after 5 minutes
- TAC: 0.1% TAC (A) then placebo (B) after 5 minutes
- N-TAC: 4% niacinamide cream (A) then 0.1% TAC (B) after 5 minutes

Patients applied the creams twice daily in a thin layer to the lesions. The treatment creams were obtained from Dermskin Cosmetics.

Data gathering procedure

Collected baseline measures (age, gender, age at disease onset, duration of disease, past psoriatic medication/s and pre-existing illness/es) PASI and PGA were based on physician observation while the DLQI was self-administered.

Psoriasis area severity index (PASI)

PASI a widely used scoring system both in patient management and clinical trials [16] was found to be correlated with the Body Surface Area (BSA) and PGA.[17] Overall, the reliability of PASI was considered good having an intra-class correlation coefficients (ICC) value of >0.75.[17]

Two blinded assessors evaluated each patient. The final PASI score for each patient was averaged. The intensity and extent of the psoriatic plaques were assessed in the four anatomical regions: head (H), trunk (T), upper (UL) and lower limb (LL). Scores assigned are seen in Table 1 below.

Table 1. Scoring for PASI

INTENSITY Erythema Thickness/ Induration Desquamation/ Scaling	EXTENT
0: none	1: 0-9%
1: mild	2: 10:29%
2: moderate	3: 30-49%
3: severe	4: 50-69%
4: very severe	5: 70-89%
	6:90-100%

The intensity of erythema (E), thickness/ induration (I) and desquamation (D) for each of the four anatomical regions (H, T, UL, and LL) were scored using a 5-point scale from 0 (none) to 4 (very severe). Meanwhile, the extent (A) of the psoriatic plaque was assessed based on the proportion of the skin affected by psoriasis on each anatomical region as scored by 1 to 6. The overall PASI score can, therefore, range from 0 to 72 by using the formula below: [17,18]

$$PASI = 0.1\,(E_H+I_H+D_H)\,A_H + 0.2\,(E_{UL}+I_{UL}+D_{UL})\,A_{UL} + + 0.3\,(E_T+I_T+D_T)\,A_T + 0.4\,(E_{LL}+I_{LL}+D_{LL})\,ALL$$

The improvement in PASI score compared to baseline and on every follow up was computed.

PASI50 equates to a clinically meaningful improvement in psoriasis, and effective widely used therapies (e.g. etanercept, alefacept) were consistently differentiated from placebo at PASI50; as such, this was considered as the primary endpoint of the study to indicate the efficacy of treatment.[19]

Physician Global Assessment (PGA)

PGA is the second tool most often used to measure psoriasis severity. [20] PGA does not consider the anatomical location and extent of psoriatic lesions. Instead, it only measures the intensity of the erythema, induration, and scaling. Nonetheless, PGA showed good reliability with an ICC of 0.87 and a good correlation with PASI. [17]

The same outcome assessors provided individually a score for the PGA. The final score was averaged. Each patient was scored as follows: 0=clear, 1=almost clear, 2=marked improvement, 3=moderate improvement, 4=slight improvement, and 5=no change and 6=worse.[17]

Dermatology Life Quality Index (DLQI)

The DLQI was used to evaluate the quality of life of the patients. It was found to be reliable (ICC=0.88 and Cronbach's alpha=0.83) and valid for psoriasis patients.[21] Patients answered 10 questions regarding their quality of life and indicated their answers in a 4-point scale: 0= not at all, 1=a little, 2=a lot, 3= very much. DLQI score ranged from 0 to 30 wherein a higher score denoted a worse quality of life.[18]

Baseline data

Baseline data included age, gender, disease onset, duration of disease, previous topical corticosteroid medication/s, underlying diseases, PASI and DLQI. The intake of multivitamins with or without vitamin B3 was not determined prior to study inclusion.

Outcome measures

PASI and PGA were assessed at 2nd, 4th, 6th, 8th and 10th week of treatment. DLQI was obtained from the patients at the beginning and at the end of the study period. Patients were instructed to contact the study coordinators for any adverse events.

Primary outcome measure: PASI score

PASI50 was considered as the primary endpoint of the study that indicated the efficacy of treatment.

Secondary outcome measures: PGA and DLQI

Assessment of clinical response was based on the differences in mean PASI scores at weeks 0, 2, 4, 6, 8 and 10. For PGA, the proportion of patients who attained a score of 0 (clear) and 1 (almost clear) were compared at the 2nd, 4th, 6th, 8th and 10th week of all treatment groups. For the DLQI, the mean reduction and improvement in scores were computed at the beginning and at the end of the treatment period.

Safety

Safety was assessed during each visit by asking for the experience of local adverse effects such as pruritus, erythema, swelling or burning sensation after the application of the test drugs.

Data Analysis

Data were encoded in MS Excel by the researcher. Stata MP version 14 was used for data processing and analysis. Continuous variables were presented as mean/SD or median/IQR depending on data distribution while categorical variables were presented as frequency/percentages. Fisher's exact test and Chi square test were used to compare the following

proportions amongst the three treatment groups: a) PASI50 and b) PGA score of 0-1. Intragroup differences in the proportion of PASI50 and PGA score of 0-1 were analyzed using Cochran's Q test. Significant Cochran's Q test results were further analyzed using McNemar's test. Comparison of treatment effect on DLQI by period was analyzed using paired t-test. Intention-to-treat analysis was implemented wherein all patients enrolled at least had 1 follow-up were included in the analysis. All p values ≤0.05 were considered statistically significant. Charts and graphs were created using MS Excel.

RESULTS

A total of 40 patients were enrolled in the study and were randomly allocated to three groups—14 in N, 13 in TAC, and 13 in N-TAC. Two patients dropped out from the study at Week 6—one from N and one from TAC. Reasons for dropout included progression to severe psoriasis and failure to show up with the follow-up schedule, respectively. Although the study failed to achieve the minimum sample size required, post-hoc analysis revealed that a sample size of 38 achieved 95% power to detect an effect size of 0.63 based on the proportion of PASI50 in groups N, TAC and N-TAC equal to 15%, 75% and 85%, respectively.

The demographic and clinical profile of patients is presented in Table 2.

Table 2. Demographic and clinical characteristics of patients (n=40)

CHARACTERISTICS	GROUP N (n=14) n(%)	GROUP TAC (n=13) n(%)	GROUP N-TAC (n=13) n(%)	P VALUE
Age (in years), mean	45.7 ± 16.5	49.8 ± 16.5	48.4 ± 12.1	0.7805
Sex				
Male	5 (36)	5 (38)	12 (92)	0.004*
Female	9 (64)	8 (62)	1 (8)	
Diabetes mellitus				
With	3 (21)	1 (8)	3 (23)	0.663
Without	11 (79)	12 (92)	10 (77)	
Dyslipidemia				
With	3 (21)	3 (23)	2 (15)	1.000
Without	11 (79)	10 (77)	11 (85)	
Cardiovascular Disease				
With	0	0	2 (15)	0.200
Without	14 (100)	13 (100)	11 (85)	
Age at psoriasis onset, mean	32.9 ± 14.5	39.2 ± 19.9	36.8 ± 14.2	0.6038
Duration of disease				
≤10 years	5 (36)	9 (69)	9 (69)	0.127
>10 years	9 (64)	4 (31)	4 (31)	
Steroid cream use				
Yes	13 (93)	11 (85)	13 (100)	0.521
No	1 (7)	2 (15)	0	
Severity of psoriasis				
Mild	12 (86)	6 (46)	7 (54)	0.069
Moderate	2 (14)	7 (54)	6 (46)	
PASI at week 0	3.88 ± 3.21	6.09 ± 4.91	6.18 ±	0.2264
DLQI at week 0	12.29 ± 5.33	8.62 ± 5.78	7.92 ± 4.86	0.0852

The mean age of the patients was 47.9 years old (range: 18-72 years old). A significantly higher proportion of males (92%) were allocated in N-TAC. No significant differences were observed amongst the pre-existing illnesses.

The mean age of psoriasis onset was 36.2 years old (range: 8-72). Only four patients (10%) developed psoriasis before the age of 18 (data not shown). A higher proportion of patients in N had psoriasis for more than 10 years as compared to other groups. Meanwhile, 37 patients (93%) reported application of topical corticosteroid for psoriasis prior to study enrollment. There were no statistically significant differences in baseline PASI and DLQI scores.

PASI

PASI50 data of patients in this study is shown in Figure 1. A significant increasing trend of PASI50 was found for TAC (p=0.0012) and N-TAC (p=0.0011) but not for N (p=0.2311).

Starting at week 4, statistically significant differences were present in the percentage of patients who achieved PASI50 amongst each treatment group. Further analysis revealed that at weeks 4 and 6, PASI50 in N and TAC were significantly lower compared to N-TAC. At weeks 8 to 10, PASI50 of N was significantly lower compared to TAC and N-TAC. At the end of the study, 85% of patients in N-TAC and 75% of patients in TAC achieved PASI50, but with no statistical significance (p=0.645, Fisher's exact test). 15% of patients in N achieved PASI 50.

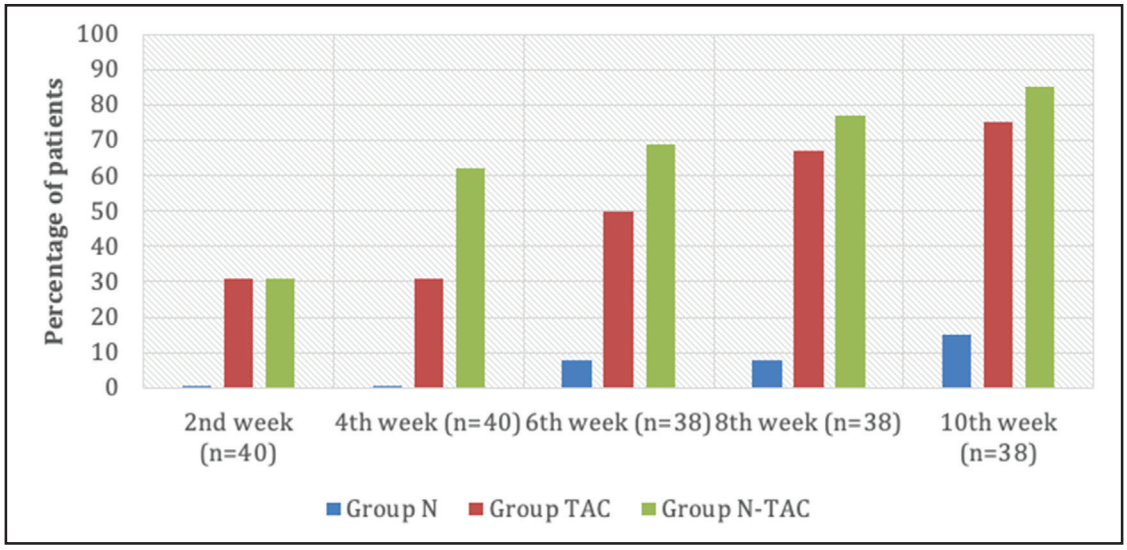
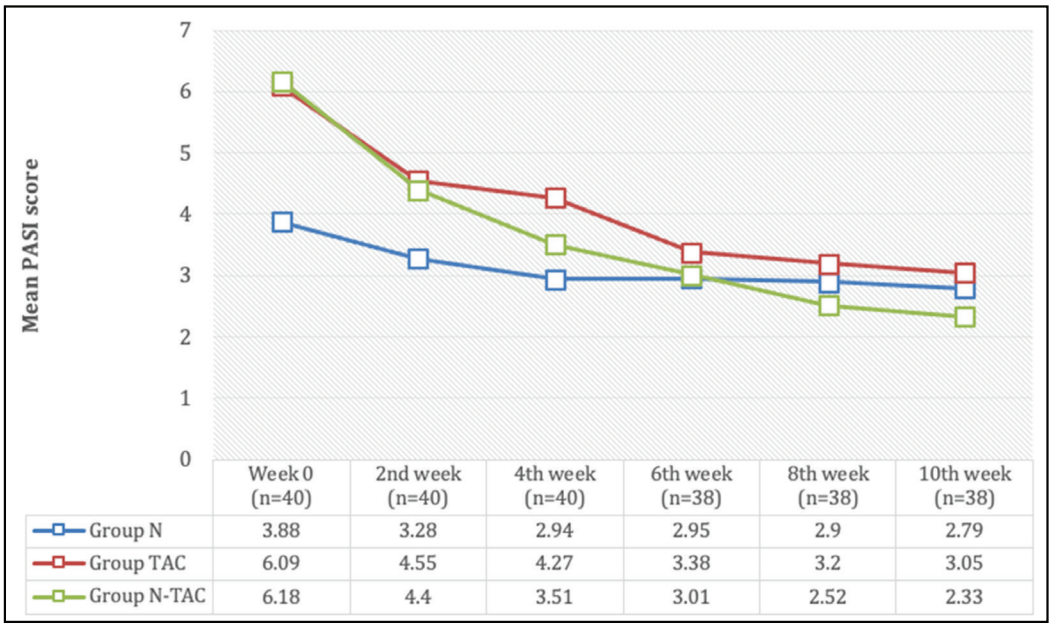


Figure 1. Percentage of patients who achieved PASI50 over time by group

Figure 2 demonstrates all study groups had improved mean PASI scores throughout the study period. Repeated Measures ANOVA showed a significant difference in mean PASI score every follow-up, as compared to baseline, for all treatment groups (all p values were <0.00001). In TAC, mean PASI scores between weeks 4 and 10 were no longer statistically significant (p=0.305). In contrast, N- TAC's mean PASI score at week 10 was still significantly different compared to week 4 (p=0.001).



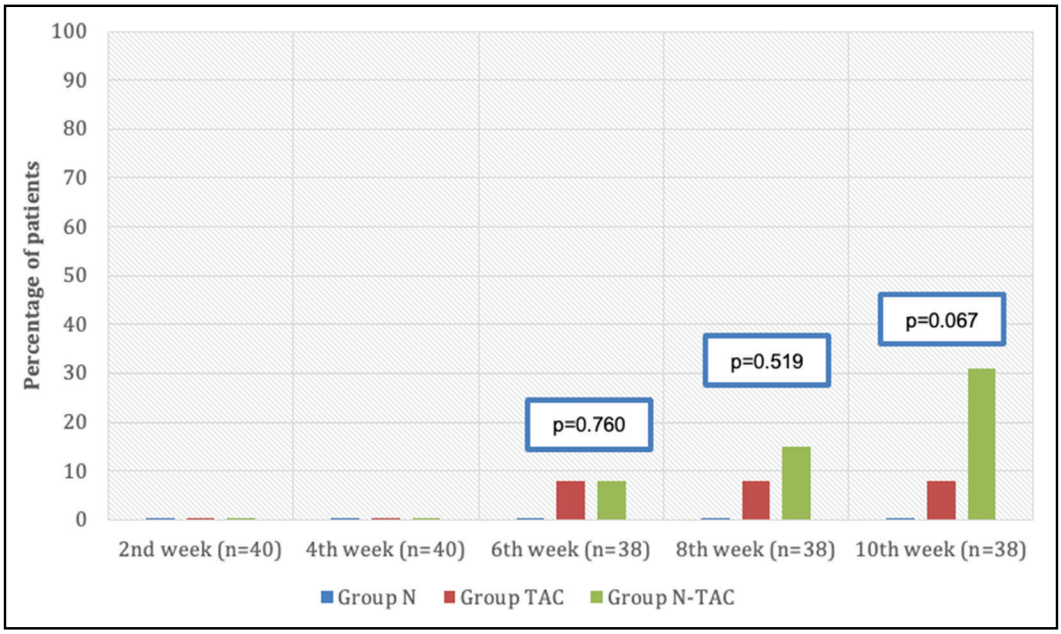
	Week 0 (n=40)	2nd week (n=40)	4th week (n=40)	6th week (n=38)	8th week (n=38)	10th week (n=38)
Group N	3.88	3.28	2.94	2.95	2.9	2.79
Group TAC	6.09	4.55	4.27	3.38	3.2	3.05
Group N-TAC	6.18	4.4	3.51	3.01	2.52	2.33

Figure 2. Percentage of patients who achieved PASI50 over time by group

PGA

Figure 3 shows the proportion of patients who were rated as being 'almost clear' of psoriatic lesions or a grade of 1 in PGA. At weeks 2 and 4, no patients in the study achieved this. At week 10, only 1 patient (8%) in TAC had a PGA score of 1. This is in contrast to N-TAC's 31% or 4 patients. However, this was not statistically significant. There was no demonstrable statistically significant difference throughout the entire study period amongst the groups with PGA score of 1 ($p>0.05$).

Figure 3. Percentage of patients who achieved PASI50 over time by group



**P values denote differences in proportion among the three treatment groups for each follow-up period*

DLQI

Figure 4 presents the improvement in DLQI score at week 10 relative to baseline amongst the three groups. Although a higher improvement in score was seen in N-TAC, mean DLQI improvement did not vary by treatment group (p=0.0770).

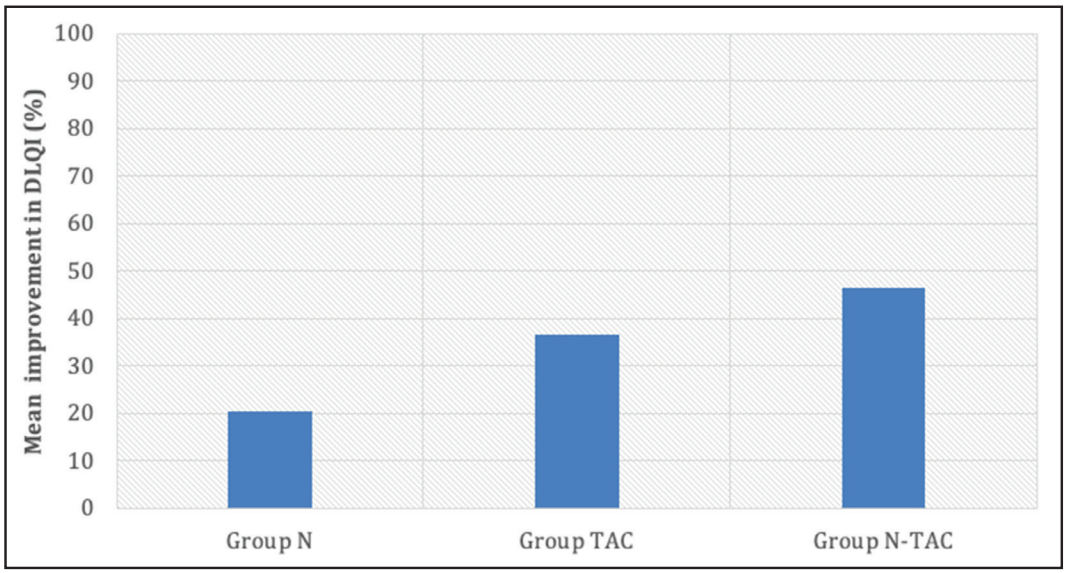


Figure 4. Mean improvement (in %) of DLQI score at Week 10 by group

ADVERSE EVENTS

All adverse events occurred in the N study group, wherein two patients had consistent minimally-graded pruritus throughout the entire treatment with no distinct eczematous lesions. Two other patients had asymptomatic minimal erythema noted at weeks 4 and 6.

Table 3. Adverse events by group and follow-up period

CHARACTERISTICS	GROUP N (n=14) n(%)	GROUP TAC (n=13) n(%)	GROUP N-TAC (n=13) n(%)	P VALUE
Pruritus				
At 2nd week	2 (14)	0	0	0.142
At 4th week	4 (29)	0	0	0.027*
At 6th week	3 (23)	0	0	0.094
At 8th week	2 (15)	0	0	0.316
At 10th week	2 (15)	0	0	0.316
Erythema				
At 2nd week	0	0	0	-
At 4th week	2 (15)	0	0	0.316
At 6th week	1 (8)	0	0	1.000
At 8th week	0	0	0	-
At 10th week	0	0	0	-

**P values denote differences in proportion among the three treatment groups for each follow-up period*

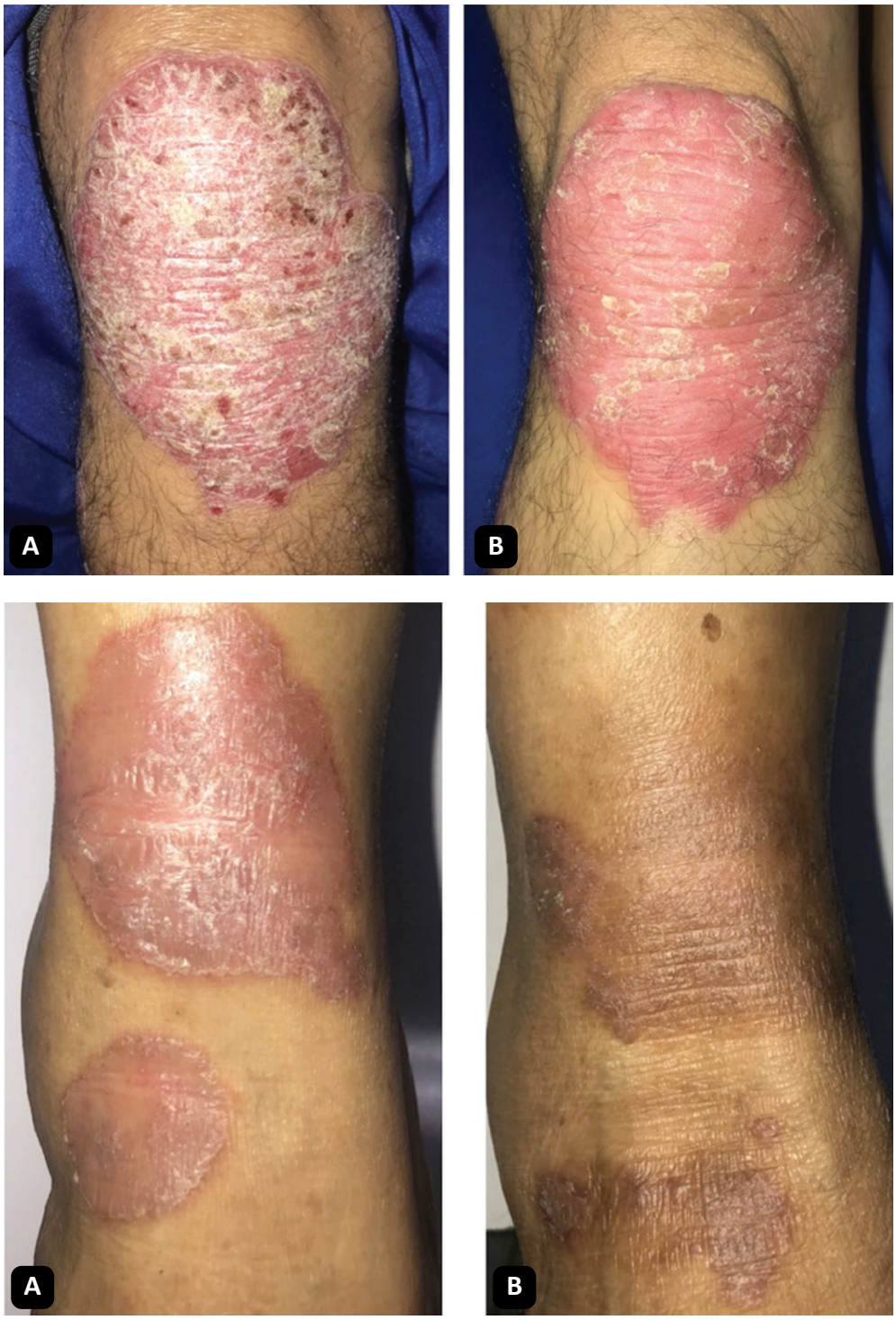

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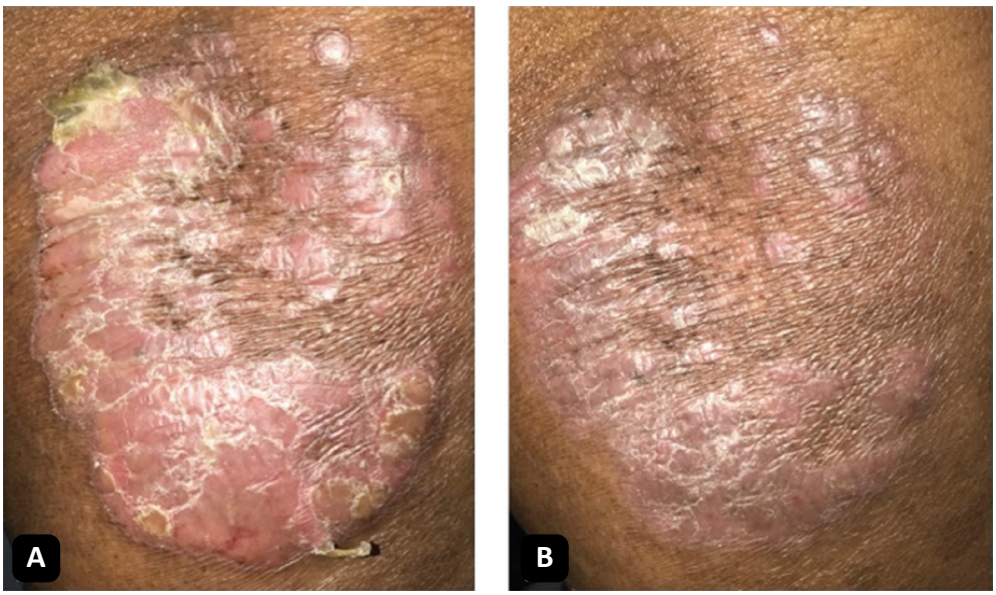
Figure 5. Treatment response of patients to 4% niacinamide cream at baseline (A) and at week 10 (B).



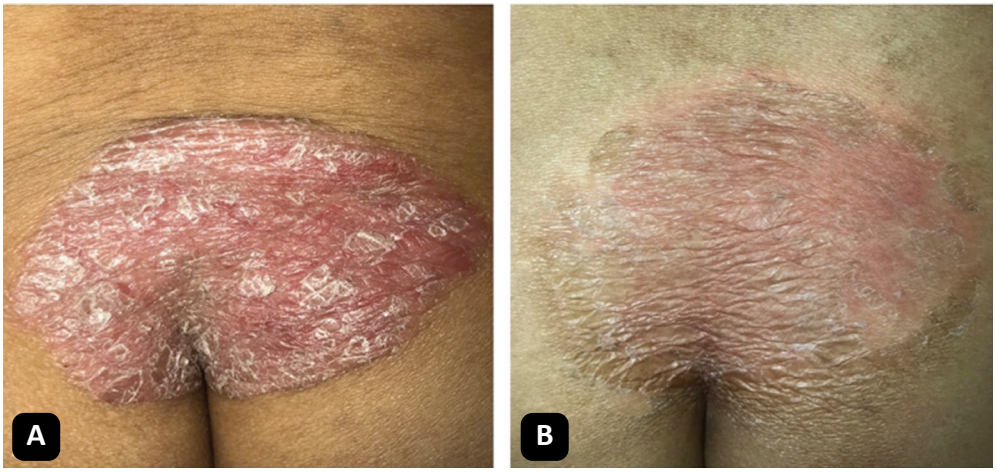
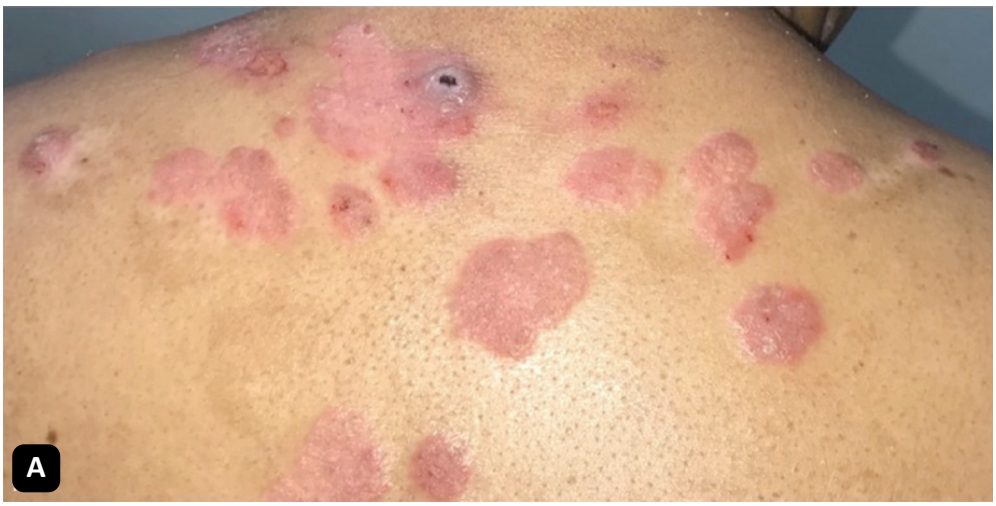


Figure 6. Treatment response of patients to 0.1% triamcinolone acetonide cream at baseline (A) and at week 10 (B).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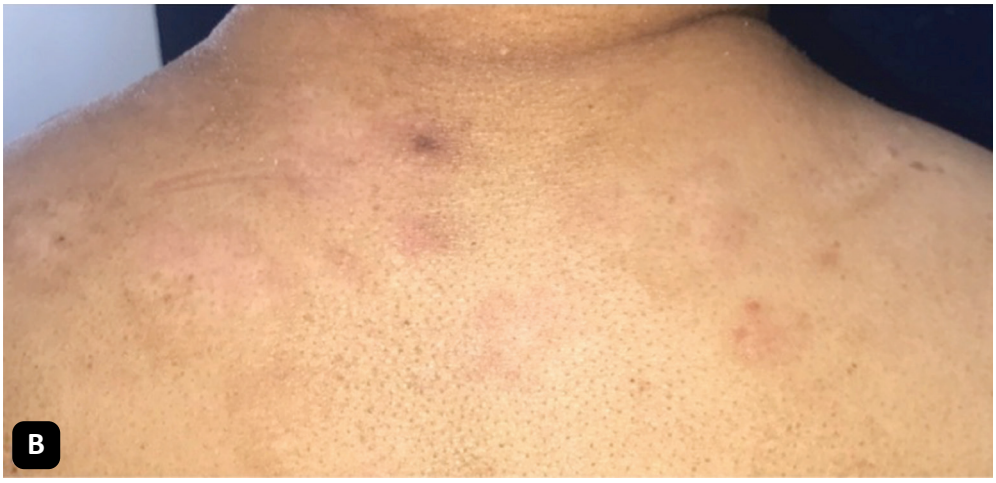
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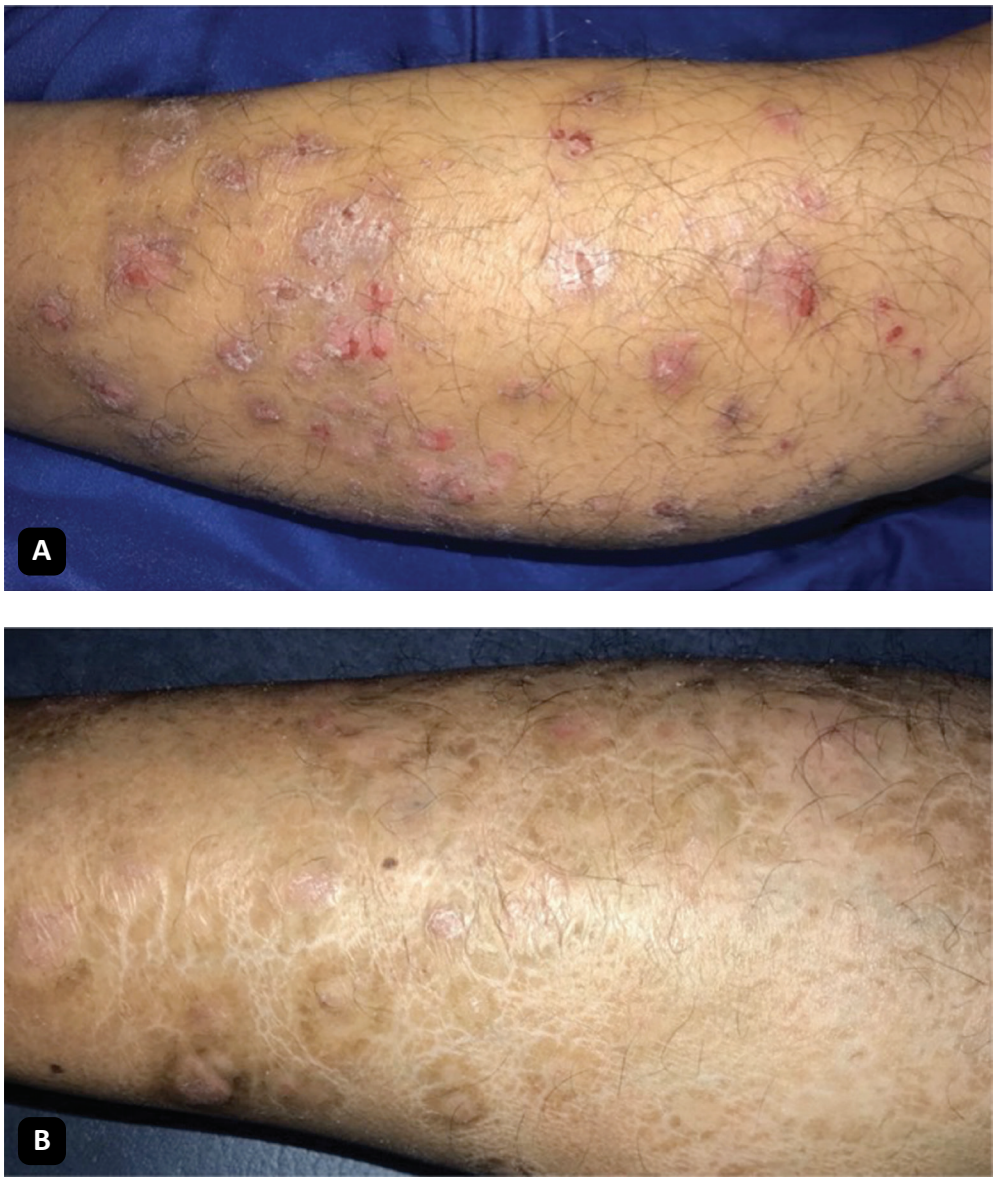

Figure 7. Treatment response of patients to 4% niacinamide cream and 0.1% triamcinolone acetonide cream at baseline (A) and at week 10 (B).

DISCUSSION

Psoriasis is a chronic disease that requires long-term management. Albeit effective in controlling symptoms and improvement in appearance, prolonged use of corticosteroids can lead to adverse events.1 Combination therapies are being explored as an alternative treatment for psoriasis that maximizes the effectiveness of corticosteroids while minimizing its side effects. Nowadays, physicians use combination treatments with topical steroids adding synergistic ingredients such as vitamin D analog (calcipotriol) and salicylic acid.22,23 A potential ingredient that gained popularity in the field of dermatology is topical niacinamide, but studies regarding its effectiveness for psoriasis are limited. 10,11

EFFICACY IN REDUCING SEVERITY

Despite the purported anti-inflammatory effect of niacinamide, the results of the study showed that topical niacinamide used as monotherapy was inferior in improving psoriatic lesions when compared to topical triamcinolone acetonide.

Topical triamcinolone acetonide's mean PASI score showed initial clinical and statistical improvement that started at week 4 which later statistically stagnated with lesions showing minimal clinical improvement. We attribute this to the possibility of tolerance or tachyphylaxis although limited evidence is available. 24–26 The exact duration of onset remains unknown. According to Taheri, et al 27, tachyphylaxis is exhibited by a heightened treatment response on the first few weeks of treatment, followed by a plateau phase depicting limited effectiveness. The same trend was observed in our study.

On the other hand, a higher number of patients who received the combination treatment N-TAC showed improvement in psoriatic lesions earlier with continued sustained improvement when compared to the usage of triamcinolone acetonide alone. This synergistic anti-inflammatory effect may be explained by niacinamide's capability to downregulate certain inflammatory markers different from corticosteroid's anti-inflammatory mechanism. 7,28–34 Niacinamide decreases expression of IL-10 and TNF-alpha as well as reduces poly- ADP ribose polymerase (PARP) and NF-kB activity.31,33,35,36 Neutrophil chemotaxis is also inhibited by niacinamide.37,38,39 Topical triamcinolone acetonide, which acts on VCAM-1, shows low permeability as 70-90% of the substance remains on the surface of the skin. This may be a problem in patients with psoriasis as the derangement of lipid synthesis leads to thickened and dry skin, thereby reducing the capacity of topical drugs to penetrate the skin barrier. 40,41 The addition of niacinamide could have increased the permeability of triamcinolone acetonide. Wan et al showed that tacrolimus permeability in the psoriatic skin was enhanced when combined with niacinamide due to the latter exhibiting moisturizing effects which would modify the barrier property and enhance the penetration of drugs.6 Siadat et al showed similar results wherein greater improvement in PASI was seen in the combination of 4% topical niacinamide with 0.005% calcipotriol11 as compared to calcipotriol alone in patients with mild to moderate psoriasis.

The efficacy of topical niacinamide with triamcinolone acetonide combination was also supported by the PGA results as 31% of patients were graded 'almost clear' of lesions at the end of the study period compared to 8% of triamcinolone acetonide alone. This is comparable with Levine et al's study wherein 50% of patients given 1.4% niacinamide with 0.005% calcipotriene achieved a rating of 'clear to almost clear' in PGA at the end of their 12-week study period compared with 25% of patients treated with 1.4% niacinamide alone, and 31.5% of patients treated with calcipotriene alone.10

EFFICACY IN IMPROVING QUALITY OF LIFE USING DLQL

Patient's perception of the impact of psoriasis in their life may differ from the actual severity based on the number of lesions. Surprisingly, even if the N group had the lowest mean PASI at baseline, their baseline DLQI were found to be the worst. This could be explained by the longer duration of their disease, such that 64% of patients had psoriasis for more than 10 years. Longer duration of psoriasis was found to be associated with worse quality of life 42 despite arguments of becoming accustomed to living with the disease. 43,44 Although a higher score improvement was seen in N-TAC, significant differences amongst the groups were not present. This may be due to the fact that patient population consisted of mild to moderate disease.

SAFETY

Mild erythema and pruritus were observed in patients given with niacinamide only. Erythema in psoriasis is said to be related to nitric oxide, which is one of the targets of corticosteroids.41 This can explain its absence in patients given with triamcinolone acetonide. Similarly, pruritus is a common symptom among patients with psoriasis. Although not considered as an anti-pruritic agent, corticosteroids indirectly control this symptom due to its effect on certain inflammatory factors. 24,45

CONCLUSION

In the 10-week treatment period, 4% niacinamide cream alone was not effective in the treatment of mild to moderate psoriasis. Erythema and pruritus were the most common side effects encountered. Both 0.1% triamcinolone acetonide cream and the combination of 4% niacinamide and 0.1% triamcinolone acetonide cream were found to be efficacious and safe in reducing symptoms. Although the effects were statistically comparable, the effect of the combination treatment resulted to a continuous and sustained improvement. No significant improvement in the quality of life was noted in all the treatment groups.

RECOMMENDATION

This paper recommends exploring a more in-depth role of niacinamide as an adjunct to other topical medications for psoriasis and as a potential steroid sparer. A larger study population with a longer study period is recommended to further study the combination of niacinamide and topical corticosteroid.

REFERENCES

1. Newman M, Weinberg J. The pathophysiology of psoriasis. In: Weinberg J, editor. Treatment of Psoriasis. 2008. p. 11–20.
2. Korman NJ, Zhao Y, Pike J, Roberts J. Relationship between psoriasis severity, clinical symptoms, quality of life and work productivity among patients in the USA. Clin Exp Dermatol. 2016;41(5):514–21.
3. Prignano F, Ricceri F, Pescitelli L, Lotti T. Itch in psoriasis: epidemiology, clinical aspects and treatment options. Clin Cosmet Investig Dermatol. 2009;2:9–13.
4. WHO. Global Report on Psoriasis. WHO Press. 2016;978(9):48.
5. Roa F. The Philippines - Treatment of Psoriasis and its Challenges. IPC PSORIASIS Rev. 2010;6(1):3–4.
6. Wan T, Pan W, Long Y, Yu K, Liu S, Ruan W, et al. Effects of nanoparticles with hydrotropic nicotinamide on tacrolimus: Permeability through psoriatic skin and antipsoriatic and antiproliferative activities. Int J Nanomedicine. 2017;12:1485–97.
7. Emanuele E, Bertona M, Altabas K, Altabas V, Alessandrini G. Anti-inflammatory effects of a topical preparation containing nicotinamide, retinol, and 7-dehydrocholesterol in patients with acne: A gene expression study. Clin Cosmet Investig Dermatol. 2012;5:33–7.
8. Washio H, Hara H, Suzuki H, Yoshida M, Hashimoto T. Bullous pemphigoid on psoriasis lesions after UVA radiation. Acta Derm Venereol. 2005;85(6):561–3.
9. Navarrete-Solís J, Castanedo-Cázares JP, Torres-Álvarez B, Oros-Ovalle C, Fuentes-Ahumada C, González FJ, et al. A double-blind, randomized clinical trial of niacinamide 4% versus hydroquinone 4% in the treatment of melasma. Dermatol Res Pr. 2011;2011:379173.
10. Levine D, Even-Chen Z, Lipets I, Pritulo OA, Svyatenko T V, Andrashko Y, et al. 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. 2010;63(5):775–81.
11. Siadat AH, Iraji F, Khodadadi M, Jary MK. Topical nicotinamide in combination with calcipotriol for the treatment of mild to moderate psoriasis: A double-blind, randomized, comparative study. Adv Biomed Res. 2013;2(2277-9175 (Electronic)):90.
12. Choonhakarn C, Busaracome P, Sripanidkulchai B, Sarakarn P. A prospective, randomized clinical trial comparing topical aloe vera with 0.1% triamcinolone acetonide in mild to moderate plaque psoriasis. J Eur Acad Dermatol Venereol. 2010;24(2):168–72.
13. Liu LS, Kang Y, Antaya R. Prospective Trial Comparing Topical Steroid Application To Wet Versus Dry Skin In Children With Atopic Dermatitis. 2014.
14. Brunner PM, Khattri S, Garcet S, Finney R, Oliva M, Dutt R, et al. A mild topical steroid leads to progressive anti-inflammatory effects in the skin of patients with moderate-to-severe atopic dermatitis. J Allergy Clin Immunol. 2016;138(April):169–78.
15. Kim DH, Lee HJ, Park CW, Kim KH, Lee KH, Ro BI, et al. The clinical efficacy of mometasone furoate in multi-lamellar emulsion for eczema: A double-blinded crossover study. Ann Dermatol. 2013;25(1):17–22.
16. Dogra S, Mahajan R. Psoriasis: Epidemiology, clinical features, co-morbidities, and clinical scoring. Indian Dermatol Online J. 2016;7(6):471.

17. Bożek A, Reich A. The reliability of three psoriasis assessment tools: Psoriasis area and severity index, body surface area and physician global assessment. Adv Clin Exp Med. 2017;26(5):851–6.

18. Schmitt J, Wozel G. The psoriasis area and severity index is the adequate criterion to define severity in chronic plaque-type psoriasis. Dermatology. 2005;210(3):194–9.

19. Carlin CS, Feldman SR, Krueger JG, Menter A, Krueger GG. A 50% reduction in the Psoriasis Area and Severity Index (PASI 50) is a clinically significant endpoint in the assessment of psoriasis. J Am Acad Dermatol. 2004;50(6):859–66.

20. Menter A, Gottlieb A, Feldman SR, Van Voorhees AS, Leonardi CL, Gordon KB, et al. Guidelines of care for the management of psoriasis and psoriatic arthritis. Section 1. Overview of psoriasis and guidelines of care for the treatment of psoriasis with biologics. J Am Acad Dermatol. 2008;58(5):826–50.

21. Badia, Mascaró, Lozano. Measuring health-related quality of life in patients with mild to moderate eczema and psoriasis: clinical validity, reliability and sensitivity to change of the DLQI. Br J Dermatol. 1999;141(4):698–702.

22. Fleming C, Ganslandt C, Guenther L, Johannesson A, Buckley C, Simon JC, et al. Calcipotriol plus betamethasone dipropionate gel compared with its active components in the same vehicle and the vehicle alone in the treatment of psoriasis vulgaris: A randomised, parallel group, double-blind, exploratory study. Eur J Dermatol. 2010;20(4):465–71.

23. Kaufmann R, Bibby AJ, Bissonnette R, Cambazard F, Chu AC, Decroix J, et al. A new calcipotriol/betamethasone dipropionate formulation (DaivobetTM) is an effective once-daily treatment for psoriasis vulgaris. Dermatology. 2002;205(4):389–93.

24. Elmariah SB, Lerner EA. Topical therapies for pruritus. Semin Cutan Med Surg. 2011;30(2):118–26.

25. Coondoo A, Phiske M, Verma S, Lahiri K. Side-effects of topical steroids: A long overdue revisit. Indian Dermatol Online J. 2014;5(4):416.

26. Rathi S, D'Souza P. Rational and ethical use of topical corticosteroids based on safety and efficacy. Indian J Dermatol. 2012;57(4):251.

27. Taheri A, Cantrell J, Feldman SR. Tachyphylaxis to topical glucocorticoids; what is the evidence? Dermatol Online J. 2013;19(7):18954.

28. Steinhoff M, Meinhardt A, Steinhoff A, Gemsa D, Bucala R, Bacher M. Evidence for a role of macrophage migration inhibitory factor in psoriatic skin disease. Br J Dermatol. 1999;141(6):1061–6.

29. Lembo S, Capasso R, Balato A, Cirillo T, Flora F, Zappia V, et al. MCP-1 in psoriatic patients: Effect of biological therapy. J Dermatolog Treat. 2014;25(1):83–6.

30. Karbach S, Croxford AL, Oelze M, Schüler R, Minwegen D, Wegner J, et al. Interleukin 17 drives vascular inflammation, endothelial dysfunction, and arterial hypertension in psoriasis-like skin disease. Arter Thromb Vasc Biol. 2014;34(12):2658–68.

31. Monfrecola G, Gaudiello F, Cirillo T, Fabbrocini G, Balato A, Lembo S. Nicotinamide downregulates gene expression of interleukin-6, interleukin-10, monocyte chemoattractant protein-1, and tumour necrosis factor-α gene expression in HaCaT keratinocytes after ultraviolet B irradiation. Clin Exp Dermatol. 2013;38(2):185–8.

32. Weiss R, Schilling E, Grahnert A, Kölling V, Dorow J, Ceglarek U, et al. Nicotinamide: A vitamin able to shift macrophage differentiation toward macrophages with restricted inflammatory features. Innate Immun. 2015;21(8):813–26.

33. Ungerstedt JS, Blombäck M, Söderström T. Nicotinamide is a potent inhibitor of proinflammatory cytokines. Clin Exp Immunol. 2003;131(1):48–52.

34. Shi Y, Zhang L, Jiang R, Chen W, Zheng W, Chen L, et al. Protective effects of nicotinamide against acetaminophen-induced acute liver injury. Int Immunopharmacol. 2012:530–7.

35. Larissa M, Lise Z, Siara Almeida Baptista T, Esteves Petersen L, Evandro Bauer M, Almeida Lopes Ungaretti C, et al. Subclinical atherogenesis in patients with mild psoriasis: A role for IL-6? Rev Assoc Med BRAs. 2017;63(9):747–52.

36. Namazi M. Nicotinamide: a potential addition to the anti-psoriatic weaponry. FASEB J. 2003;17(11):1377–9.

37. Fernandes CA, Fievez L, Ucakar B, Neyrinck AM, Fillee C, Huaux F, et al. Nicotinamide enhances apoptosis of G(M)-CSF-treated neutrophils and attenuates endotoxin-induced airway inflammation in mice. Am J Physiol Lung Cell Mol Physiol. 2011;300(3):L354-61.

38. Wiecher JW, Drenth BFH, Jonkman JHG, de Zeeuw RA. Percutaneous absorption of triamcinolone acetonide from creams with and without Azone®in humans in vivo. Int J Pharm. 1990;66(1–3):53–62.

39. Schaefer H, Zesch A, Stüttgen G. Penetration, permeation, and absorption of triamcinolone acetonide in Normal and Psoriatic Skin. Arch Dermatological Res. 1977;258(3):241–9.

40. Wolf R, Orion E, Ruocco E, Ruocco V. Abnormal epidermal barrier in the pathogenesis of psoriasis. Clin Dermatol. 2012:323–8.

41. Uva L, Miguel D, Pinheiro C, Antunes J, Cruz D, Ferreira J, et al. Mechanisms of action of topical corticosteroids in psoriasis. Int J Endocrinol. 2012;2012:561018.

42. Chen C-Y, Marrone G, He Z-H. Health Quality of Life and its associated factors for psoriasis patients in China: a cross-sectional study from hospital-based data. Karolinska Institutet, 2016.

43. Eida A, Elweshahi H. Quality of life of Egyptian patients with psoriasis: a hospital based cross-sectional survey. Egypt J Dermatology Venerol. 2016;36(1):11.

44. Lee YW, Park EJ, Kwon IH, Kim KH, Kim KJ. Impact of psoriasis on quality of life: Relationship between clinical response to therapy and change in health-related quality of life. Ann Dermatol. 2010;22(4):389–96.

45. Patel T, Yosipovitch G. Therapy of pruritus. Expert Opin Pharmacother. 2010;11(10):1673–82.