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

By

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ABSTRACT

Background: Psoriasis is a chronic skin disorder typically characterized by symmetrical erythematosus 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, photoprotective, 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-
EVALUATION OF EFFICACY AND SAFETY OF TOPIC AL...

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:**


**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 16 males (53%) and 14 females (43%). Their ages range from 18 to 66 years (Mean ±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 (17 males), (13 females) 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

<table>
<thead>
<tr>
<th>Demographic data</th>
<th>Groups</th>
<th>Group I (N = 30)</th>
<th>Group II (N = 30)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Sex</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td></td>
<td>16</td>
<td>17</td>
<td>0.795</td>
</tr>
<tr>
<td>Female</td>
<td></td>
<td>14</td>
<td>13</td>
<td></td>
</tr>
<tr>
<td><strong>Age (years)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean ±SD</td>
<td></td>
<td>41.7 ± 15.5</td>
<td>42.3 ± 11.4</td>
<td>0.857</td>
</tr>
<tr>
<td><strong>Duration (years)</strong></td>
<td></td>
<td>4.3 ± 2.6</td>
<td>3.4 ± 2.8</td>
<td>0.084</td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Groups</th>
<th>PASI Score</th>
<th>Before (N = 30)</th>
<th>After (N = 30)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group I</td>
<td>Mean ±SD</td>
<td>14.9 ± 7.8</td>
<td>11.1 ± 6.7</td>
<td>0.023</td>
</tr>
<tr>
<td></td>
<td>Median</td>
<td>14.2</td>
<td>9.75</td>
<td></td>
</tr>
<tr>
<td>Group II</td>
<td>Mean ±SD</td>
<td>16.2 ± 5.05</td>
<td>9.01 ± 3.2</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td></td>
<td>Median</td>
<td>16.5</td>
<td>8.6</td>
<td></td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Groups</th>
<th>Group I (N = 30)</th>
<th>Group II (N = 30)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>DLQI score</td>
<td>Mean ±SD</td>
<td>7.6 ± 3.8</td>
<td>16.7 ± 4.5</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td></td>
<td>Median</td>
<td>7</td>
<td>18</td>
<td></td>
</tr>
<tr>
<td>DLQI score categories</td>
<td>No effect</td>
<td>3 10%</td>
<td>0 0%</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td></td>
<td>Small effect</td>
<td>5 16.7%</td>
<td>0 0%</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Moderate effect</td>
<td>15 50%</td>
<td>5 16.7%</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Very large effect</td>
<td>7 23.3%</td>
<td>25 83.3%</td>
<td></td>
</tr>
</tbody>
</table>

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.
AHMED SAEED MOSTAFA ANBAR et al.,

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**


EVALUATION OF EFFICACY AND SAFETY OF TOPICAL...

1423

تقييم فعالية وأمان النيكوتيناميد الموضعي في مرضى الصدفية مقارنة بالكالسيبوترييول بيتياميثازون (دراسة مقارنة)

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خلفية البحث: يُعد مرض الصدفية مرضًا جلديًا يحدث عندما تتسارع دورة حياة خلايا الجلد. تتسبب الصدفية في ترتكب خلايا الجلد الزائدة الناتجة عن القشرة والبقع البحرريحة تشعر أحيانًا بالحكة والألم. تختلف علامات وأعراض الصدفية من شخص لآخر. وتشير العديد من الأعراض والعلامات الشائعة إلى أن يمكن أن تظهر علامات الشائعة الصغرى (تظاهر عادة لدى الأطفال) وبشرة جافة ومشققة قد تننزف، الحكة أو الحرقان ووجع وأطفر سمكة أو مقدرة أو مجعدة وعاصفة متورمة ومثبسة.

ويُعد مرض الصدفية مرضًا مزمنًا والذي غالبًا يظهر ويختفي ويتكرر. المهم من العلاج هو منع نمو خلايا الجلد بشكل سريع.

الهدف من البحث: تقييم فعالية وسلامة النيكوتيناميد الموضعي لعلاج مرضى الصدفية في دراسة التجارب السريرية التداخلية مقارنة مع كالسيبوترييول بيتياميثازون.

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

المجموعة الأولى: استخدمت النيكوتينامين الموضعي 4% والمجموعة الثانية: استخدمت الكالسيبينتريلول وتتم متابعة المرضى أسبوعيا لمدة ثلاثة أشهر وتقييم مستوي فعاليته ودوره في علاج مرض الصدفية.

نتائج البحث: استخدم الكالسيبينتريلول الموضعي أكثر فعالية وأمانا في العلاج مقارنة باستخدام النيكوتيناميد الموضعي مع وجود أعراض جانبية أقل.

الاستنتاج: استخدم الكالسيبينتريلول الموضعي أكثر فعالية وأمانا في علاج مرضى الصدفية مقارنة باستخدام النيكوتيناميد الموضعي مع وجود أعراض جانبية أقل، مع التوصية بعمل مزيد من الدراسات على علاج النيكوتيناميد الموضعي واستخدامه في مرضى أكثر في دراسات مستقبلية.