THE CLINICAL EFFICACY OF TOPICAL CALCIPOTRIOL AND METHYLPREDNISOLONE ACEPONATE IN CHRONIC PLAQUE PSORIASIS

KRONİK PLAK PSORİAZİSDE TOPİKAL KALSİPOTRİOL VE METİLPREDNİZOLON ASEPONATIN KLİNİK ETKİNLİKLERİ

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Gazi Medical Journal 2003; 14: 175-179

ABSTRACT

Purpose: *To assess the clinical efficacy of calcipotriol and methylprednisolone aseponate ointments in the treatment of chronic plaque psoriasis.* ***Methods:*** *This study involved 30 patients with stable and moderate severity chronic plaque psoriasis. The patients were divided into 2 treatment groups and administered calcipotriol ointment or methylprednisolone aseponate (MPA) ointment twice daily for 6 weeks. The Psoriasis Area and Severity Index (PASI) scoring system was used for the clinical evaluation. Pre-treatment and post-treatment PASI scores were compared.* ***Results:*** *In the calcipotriol group, the mean of pre-treatment PASI scores was 9.98 ± 1.76 and the mean of post-treatment PASI scores was 3.04 ± 0.88. The difference was statistically significant ($p<0.05$). MPA treatment achieved a fall in the mean PASI score from 10.13 ± 1.65 to 2.13 ± 1.65, and the difference was statistically significant ($p<0.05$). No significant differences were found between the 2 groups at the end of treatment with respect to PASI scores ($p>0.05$).* ***Conclusion:*** *Calcipotriol ointment is a safe and efficient treatment modality for chronic plaque psoriasis when it is used twice daily for 6 weeks, and is a good and safe alternative to MPA ointment in the treatment of the disease.*

Key Words: *Calcipotriol, Methylprednisolone Aseponate, Psoriasis, Topical Therapy.*

ÖZET

Amaç: *Kronik plak psoriazis tedavisinde kalsipotriol ve metilprednizolon aseponat pomadın klinik etkinliklerini karşılaştırmak.* ***Materyal ve Metod:*** *Çalışmaya stabil ve kronik plak psoriazisi bulunan 30 hasta alındı. Olgular iki gruba ayrılarak kalsipotriol pomad ve metilprednizolon aseponat (MPA) tedavilerini günde iki kez 6 hafta süreyle kullandılar. İlaçların klinik etkinlikleri Psoriasis Area and Severity Index (PASI) Skoru kullanılarak değerlendirildi. Tedavi öncesi ve sonrası PASI skorları istatistiksel olarak karşılaştırıldı.* ***Bulgular:*** *Kalsipotriol grubunda tedavi öncesi PASI skoru ortalaması 9.98 ± 1.76 ve tedavi sonrası 3.04 ± 0.88 idi ve aradaki fark istatistiksel olarak anlamlıydı ($p<0.05$). MPA tedavisi ile PASI skoru 10.13 ± 1.65'den 2.13 ± 1.65'e indi, aradaki fark istatistiksel olarak anlamlıydı ($p<0.05$). Tedavi sonunda her iki grup arasında PASI skoru değerleri bakımından istatistiksel olarak anlamlı bir fark yoktu ($p>0.05$).* ***Sonuçlar:*** *Günde iki kez altı hafta süreyle kullanılan kalsipotriol pomad kronik plak psoriazis tedavisinde etkili ve güvenilir bir tedavi seçeneği olup, psoriazis tedavisinde MPA pomada güvenilir bir alternatiftir.*

Anahtar Kelimeler: *Kalsipotriol, Metilprednizolon Aseponat, Psoriazis, Topikal Tedavi.*

INTRODUCTION

Psoriasis is a common, chronic inflammatory dermatological disorder characterized by well-demarcated indurated, red papules and plaques with white-silvery scales (1). Psoriasis patients comprise about 6-8% of the patient load in a dermatology clinic (2). Psoriasis has a worldwide distribution with prevalence varying according to race and geographical location. In epidemiological studies, the prevalence of psoriasis is reported to be between 0.1% and 3% (3-5).

In 70% of patients with psoriasis, topical therapies are effective in maintaining control of

the disease (6). Topical treatment of psoriasis is quick and safe under certain circumstances. Topical therapies include emollients, keratolytics, anthralin, tar, calcipotriol, topical steroids and retinoids (2, 6, 7).

Topical corticosteroids remain one of the most widely used treatment modalities for psoriasis, but they have side effects that limit their long-term use (7-15). Vitamin D analogues are an alternative to topical corticosteroid in the topical therapy of psoriasis, and their value has been confirmed with double-blind, right/left comparison, placebo-controlled studies (16-23). Studies have shown that calcipotriol is as effective as or superior to betamethasone valerate ointment in clearing psoriasis (6). Calcipotriol has also been shown to be superior to tar and short-contact dithranol therapy (23, 24). The aim of this study was to compare the effectiveness of calcipotriol ointment with that of methylprednisolone aseponate (MPA) in the therapy of stable psoriasis.

MATERIALS AND METHODS

A. Subjects: This study involved 30 patients (age 21-45 years, mean age: 32.50 ± 6.71 years) of both sexes with stable and moderate (Psoriasis Area and Severity Index (PASI) score less than 15) chronic plaque psoriasis. None of the patients had scalp involvement. All patients' diagnosis of psoriasis was confirmed by clinical and histopathological findings. All patients had discontinued topical antipsoriatic medication at least 2 weeks prior to the pre-trial assessment. Likewise, 4 weeks before the pre-trial assessment, the patients had discontinued any systemic antipsoriatic medication.

During this pre-trial period, the patients underwent hemoglobin, white cell count, hematocrit, sedimentation rate, blood glucose, liver function, creatinine, uric acid, sodium, potassium, calcium and phosphorus tests, and urinary analysis, and those having normal results were enrolled in the study.

Patients were informed about the study, and all provided their written informed consent.

B. Design: This study was conducted at Gazi University Faculty of Medicine, Department of Dermatology between January 2000 and February 2002. The disease was diagnosed according to clinical and histopathological features. The patients were divided in 2 treatment groups. Fifteen patients applied calcipotriol ointment, and the other 15 patients applied MPA ointment for 6 weeks. Patients were instructed to apply the ointments twice daily in a thin layer, and only to psoriatic lesions. Occlusion was not permitted. The maximum dose of calcipotriol is 100 g per week (6, 25-28) and in our study our use did not exceed 50 g per week for safety purposes. During the 6-week treatment period, the patients were seen every week; however, the PASI score was assessed only before and at the end of the study.

B. Assessment: The study groups were evaluated according to age, sex and clinical features. The PASI was used for the clinical evaluation. PASI score is also used for defining the clinical severity of the psoriasis: PASI<3: mild psoriasis, 3<PASI<15: moderate psoriasis, PASI>15: severe psoriasis (17, 29).

C. Statistical Analysis: The Statistical Program for Social Sciences 11.0 (SPSS 11.0) was used for statistical analysis. The Mann-Whitney U test was used for age and sex comparison and the Wilcoxon signed rank test was used to assess changes in PASI scores.

RESULTS

A. Subjects: Thirty patients were recruited, 15 in each group. In the calcipotriol group there were 8 (53.3%) females and 7 (46.7%) males. The mean age of the patients was 32.60 ± 6.44 years (range 21-45 years). In the MPA group there were 9 (60%) females and 6 (40%) males. The mean age of the patients was 32.40 ± 6.99 years (range 23-45 years). No statistical differences were found between the 2 groups according to age and sex analysis ($p>0.05$) (Table 1).

B. PASI scores: In the calcipotriol group, the mean of pre-treatment PASI scores was 9.98 ± 1.76 and the mean of post-treatment PASI scores was 3.04 ± 0.88. The difference was statistically significant ($p<0.05$). MPA treatment achieved a fall in the PASI score from 10.13 ± 1.65 to 2.13 ± 1.65, and the difference was statistically significant ($p<0.05$). No significant differences were found at the end of treatment between the 2 groups with respect to PASI scores ($p>0.05$). The mean decrease in PASI scores was 69.53% for the

calcipotriol group and 78.97% for the MPA group ($p<0.05$) (Table 1).

Table-1: The statistical analysis of the treatment groups.

	Calcipotriol Group		MPA Group		P value
Age (years)	32.60 ± 6.44		32.4 ± 6.99		>0.05
Sex (F/M)	8/7		9/6		>0.05
PASI score					
Pre-treatment	9.98 ± 1.76		10.13 ± 1.65		>0.05
		<0.05*		<0.05*	
Post-treatment	3.04 ± 0.88		2.13 ± 1.65		>0.05

* The statistical analysis between pre-treatment and post-treatment scores.

Table-2: The effectiveness of calcipotriol in the treatment of psoriasis.

Study	Patients (n)	PASI score Pre-treatment	Post-Treatment	Improvement rate (%)	Duration (weeks)
Van de Kerkhof et al. (17)	88	17.1	7.28	57.4	4
Gianotti et al. (20)	40	8.3	4.29	51.8	4
Park et al. (21)	12	18.4	6.5	64.7	8
Kragballe et al. (22)	174	8.36	2.7	67.7	6
Tham et al. (23)	30	6.6	2	69.8	6
Kaur et al. (24)	10	2.14	0.71	66.8	8
Bourke et al. (28)	16	25	7.9	68.4	2
Savoia et al. (32)	7	6.86	1.38	79.88	8
Douglas et al. (33)	369	10.9	2.5	65.3	6

DISCUSSION

Psoriasis is a common, chronic, inflammatory dermatological disorder characterized by hyperproliferation, and resistance of keratinocytes to apoptosis, possibly at the level of T cell-keratinocyte interaction. Although the etiology of psoriasis remains unknown, it is thought that it develops as a result of immunological abnormalities probably restricted to the skin in genetically predisposed subjects (1, 3, 30).

The synthesis of the vitamin D analogue calcipotriol was first reported in 1987, and since then it has become the most widely studied vitamin D analogue (18, 19, 27, 31). It shows its effects either by nuclear receptors or transmembrane signaling. In psoriasis, calcipotriol inhibits the cytokine synthesis of keratinocytes and other dermal cells, and modulates immune responses, proliferation and differentiation (26, 32).

The effectiveness and safety of calcipotriol ointment (50 µ/g), up to 100 g/week in the treatment of chronic plaque psoriasis, have been reported in 3-8-week trials (17, 20-24, 28, 33). Our results confirm the effectiveness of topical calcipotriol in chronic plaque psoriasis. After 6 weeks of treatment with calcipotriol, the reduction in the PASI score was 69.53%. This is in agreement with other studies, which showed a reduction of between 50 and 70%, when used for 2-8 weeks twice daily (Table 2)(17, 20-24, 28, 32, 33). A mean fall of 57.4% in the PASI after 4 weeks of therapy was found by Van de Kerkhof et al., and they hypothesized that calcipotriol response had a slow onset (17). The response rates of 69.69% at 6 weeks and 94% at 8 weeks in other studies also supported their hypothesis (22, 28, 33, 34). Furthermore, studies have shown that calcipotriol achieves similar (64.7-69.4%) improvement rates either when used for longer periods (8 weeks) in standard doses or for shorter periods (2 weeks) in higher doses (21, 28).

Topical corticosteroids are widely used in the treatment of psoriasis. They have vasoconstrictive, anti-inflammatory, antiproliferative and immunosuppressive effects (9, 14, 15, 35). This is why they are the mainstay of psoriasis therapy (15). The side effects related to topical steroid use (atrophy, striae, acne, perioral dermatitis, hypopigmentation, folliculitis, rebound phenomenon etc.) reduce their value in topical therapy (11). Topical glucocorticoids with improved benefit/risk ratios are of great interest in dermatology (15). MPA is one of these newer preparations (10). In many trials, it is well documented that its efficacy is

comparable to that of potent steroids, while its side effects are comparable to those of weak steroids. MPA has a much greater vasoconstrictor effect than hydrocortisone and is 100 times more potent. The anti-inflammatory effect of MPA is comparable to that of diflocortolon 21-valerate (10). In contrast, its side effects are as mild as those of hydrocortisone (10, 11). Percutaneous absorption of MPA through intact skin is small (<1%) and this prevents systemic absorption and side effects (12, 13).

The mean fall of 78.97% in the PASI with MPA in our patients was comparable to the results of other studies with potent steroids (10-12, 36). Douglas et al. found a mean decrease of 61% in PASI scores for betametasone dipropionate in 372 patients at the end of 6 weeks (33). These findings also confirm that MPA is a potent steroid. No side effects related to topical steroid use were observed in our patients and this result is in agreement with previous studies (11).

Calcipotriol has been shown to be superior to tar and dithranol, and its effectiveness is comparable to that of potent steroids in the treatment of chronic plaque psoriasis (6, 23, 24). In previous studies, calcipotriol was found to be more effective than steroids after 6 weeks of therapy (6), but in our study the improvement rates favor MPA. As the mean fall in the PASI score for our calcipotriol patients was in agreement with previous studies, we thought that this difference is related to MPA's potency. In addition, the rapid response to steroid therapy and/or the slow onset of response to calcipotriol therapy may have contributed to this result (8, 12, 15, 17). There was no difference in the mean PASI scores between the 2 groups at the end of the study, and this showed the effectiveness of calcipotriol in the treatment of psoriasis. Considering the chronic course of psoriasis and the side effects of corticosteroids, calcipotriol can be an alternative.

In conclusion, calcipotriol ointment is a safe and efficacious treatment modality for chronic plaque psoriasis when used twice daily for 6 weeks, and it is a good and safe alternative to MPA ointment in the treatment of the disease.

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