

Non-invasive Evaluation of Topical Calcipotriol versus Clobetasol in the Treatment of Psoriasis

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Topical treatment of psoriasis with calcipotriol has been proven effective. The efficacy of calcipotriol has been compared to that of topical corticoids in a number of studies using subjective visual scoring systems such as the PASI index.

The purpose of this study was to compare, with objective data, the efficacy of calcipotriol and clobetasol propionate 0.05% in the treatment of plaque type psoriasis.

Transepidermal water loss (TEWL) and laser Doppler velocimetry (LDV) were used to monitor restoration of water barrier and normalization of blood flow, respectively, in psoriatic plaques of the limbs of 24 male patients during 3 weeks of treatment. Data were compared to subjective evaluation using the PASI index of the same areas.

Significant differences were recorded during treatment in both groups. The results correlated well with the PASI score. Clobetasol was faster in restoring barrier function than calcipotriol. However, no significant differences were detected between the two groups.

The use of vitamin analogues may be effective in the topical treatment of psoriasis by normalizing skin biophysical parameters and minimizing the risks of side-effects induced by potent topical corticoids. **Key words:** TEWL; laser Doppler velocimetry.

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Psoriasis is a recurrent dermatosis where topical treatment is characterized by a high risk of failure and side-effects. An important step in the topical treatment of this disease is the use of calcipotriol, a new vitamin D analogue. This class of compounds, particularly calcipotriol, have been shown to have an antiproliferative effect on cultured keratinocytes (1); Holland et al. (2) found that topical treatment with calcipotriol reduced epidermal hyperproliferation and restored normal turnover after 10 weeks in psoriatic epidermis. Other effects of calcipotriol

include downregulation of IL-1, IL-6 and T cell activation (3, 4). Recently, the effects on cytokeratins and immune system in psoriatic patients were investigated comparing the efficacy of calcipotriol and betamethasone valerate (5): both treatments showed a reduction of T lymphocytes, HLA-DR cells and keratin K₁₆.

The clinical efficacy of calcipotriol has been evaluated in a number of studies (6, 7) quantifying visually erythema, desquamation, and thickness of psoriatic plaques. However, visual scoring is related to the subjective evaluation of the clinician and may not be useful in differentiating between two treatments. In this study, we have compared calcipotriol and 0.1% clobetasol in the treatment of psoriasis; healing of plaques was evaluated both by visual score and instrumentally by laser Doppler velocimetry (LDV) and transepidermal water loss (TEWL).

MATERIALS AND METHODS

Twenty-four male patients (age 25–84, mean 57.5) affected by plaque type psoriasis of the limbs entered the study after giving their informed consent. They were not receiving any other treatment (topical or systemic) for psoriasis or other diseases that could interfere with topical treatment (lithium, beta-blockers, corticosteroids). The subjects included had discontinued every topic, or systemic treatment for psoriasis (including UV only) since 2 months. Subjects with hypercalcemia, liver diseases with liver enzymes above 50% of normal values, or UV exposure, were excluded from the study. In each subject one plaque on the elbow (left or right, randomly) was selected for instrumental follow-up.

Twelve subjects were treated with calcipotriol ointment 50 µg/g and 12 with clobetasol propionate 0.05% in cream twice a day for 3 weeks.

One cm of cream was evenly applied on a surface of 100 cm². Visual assessment of psoriatic plaques was performed before and at the end of the study. Instrumental assessment was performed under basal conditions and during treatment every week for 3 weeks. Visual scoring the severity of the disease was evaluated according to the degree of erythema, thickness and scaling (0 = none, 3 = severe). A total sign score was obtained by averaging the values.

Instrumental assessment: the recovery of barrier function properties and the formation of efficient stratum corneum were measured using an

Table I. TEWL and LDV values during treatment with topical clobetasol and calcipotriol

TEWL is expressed in g m²/h, LDV in % of blood flow.

	Clobetasol		Calcipotriol	
	TEWL	LDV	TEWL	LDV
Baseline	22.2 ± 8.2	240.6 ± 167	28.3 ± 8.5	295.2 ± 255
Week 1	22.1 ± 8.4	158.6 ± 112*	25.0 ± 8.4	240.9 ± 230
Week 2	13.8 ± 5.0*	107.0 ± 70*	23.5 ± 8.2	182.1 ± 176
Week 3	11.8 ± 4.2*	108.8 ± 101*	19.7 ± 6.0*	120.3 ± 126*

* Significant differences at the 0.05% level compared to baseline (see text for details)

Table II. Visual score before and after 3 weeks of treatment

Both treatments induced a significant improvement of clinical conditions ($p < 0.01$).

	Clobetasol	Calcipotriol
Baseline	3.0 ± 0.0	2.94 ± 0.12
Week 3	0.056 ± 0.1	1.36 ± 0.6

evaporimeter (Ep-1 Servomed, Kinna, Sweden); it is known that this technique is useful in monitoring psoriatic treatment (8, 9). TEWL measurements were taken according to guidelines suggested for this technique (10); improvement of skin microcirculation with reduction of vasodilatation and papillomatosis underneath the psoriatic plaque was monitored by measurements of skin blood flow using LDV (11). A decrease in blood flow can sometimes precede the healing of a psoriatic plaque and is related to the effectiveness of the treatment (12). Blood flow was measured using the Periflux (Perimed, Sweden) PF IIB laser Doppler velocimeter connected with a Toshiba 3200 SX computer with dedicated software (Perisoft Diastron limited, UK) to analyze tissue perfusion. To avoid the effects of large scales on the recordings, psoriatic lesions were treated for 24–48 h with 5% salicylic ointment to remove hyperkeratosis only before taking baseline recordings.

Statistical analysis of the data was performed using analysis of variance for repeated measures, Fisher PLSD and unpaired Student's *t*-test and Pearson's correlation.

RESULTS

Results are shown in Tables I, II and III and Fig. 1. Both treatments induced a significant decrease of TEWL and LDV as well as visual scoring (Tables I and II). In the group treated with calcipotriol, significant differences during the treatments were found (ANOVA = $p < 0.01$ for TEWL and $p < 0.03$ for LDV).

Multiple comparisons showed significant differences between the baseline and week 3 for both TEWL and LDV ($p < 0.05$); the group treated with clobetasol showed higher statistical significance (ANOVA = $p < 0.0001$ for TEWL and $p < 0.0007$ for LDV). Multiple comparisons showed ($p < 0.05$) significant differences for TEWL between baseline and week 2 and 3 and week 1 vs week 2 and 3 and significant differences for LDV between baseline and week 2 and 3. Direct comparison between the two groups is shown in Table III. Treatment with clobetasol resulted in a significant reduction of TEWL compared to calcipotriol at weeks 2 and 3. No differences were found between the two groups as measured by LDV. Correlation between visual score and instrumental evaluation was significant (Fig. 1, $r = 0.618$ ($p < 0.0001$) for TEWL and $r = 0.342$ ($p < 0.01$) for LDV).

DISCUSSION

Staberg et al. (13) measured blood flow in psoriatic plaques and found a reduction after 2 weeks of topical treatment with calcipotriol compared to base cream. The data correlated well with clinical evaluation; interestingly, also base cream improved blood flow and clinical score. In our study calcipotriol (50 µg/g) was compared to a potent corticosteroid (clobetasol), which is the most powerful corticoid available for topical use in dermatology.

From a clinical viewpoint, both calcipotriol and clobetasol resulted in a significant ($p < 0.01$) improvement of psoriatic

Table III. Direct comparison between the calcipotriol and the clobetasol group

Significant differences were recorded with TEWL measurements at weeks 2 and 3.

	Calcipotriol vs Clobetasol : Statistical differences in instrumental evaluation	
	TEWL	LDV
Baseline	n.s.	n.s.
Week 1	n.s.	n.s.
Week 2	0.002	n.s.
Week 3	0.001	n.s.

plaques and visual score (Table II). No significant differences were detected between the two treatments.

Both treatments induced a significant decrease in TEWL during treatment ($p < 0.01$ for calcipotriol and $p < 0.0001$ for clobetasol). The improvement was significant from week 2 in the clobetasol group and at week 3 in the calcipotriol group (Table I). Indeed, lateral comparison between the two groups showed significant changes from week 2 onwards (Table III, $p < 0.002$ and $p < 0.001$ at week 2 and 3, respectively). Clobetasol is more efficient than calcipotriol in restoring barrier function; the anti-inflammatory and antimetabolic effects of this powerful corticoid reduce epidermal proliferation earlier than calcipotriol, leading to the formation of normal keratin which significantly improves barrier function after 2 weeks of treatment. On the other hand, no important differences were found between the two groups as measured by LDV. A significant reduction of blood flow was recorded in both groups (Table I, $p < 0.03$ for calcipotriol and $p < 0.007$ for clobetasol). Multiple comparison statistics show that blood flow appears significantly lower after week 1 in the group treated with clobetasol (Table I); however, lateral comparisons (Table III) show no significant differences between the groups; at week 3 blood flow levels are equal in the two groups. The earlier effect in reduction of blood flow, noticed in the clobetasol group, is consistent with the vasoconstrictive activity of corticosteroids. At this stage, vaso-

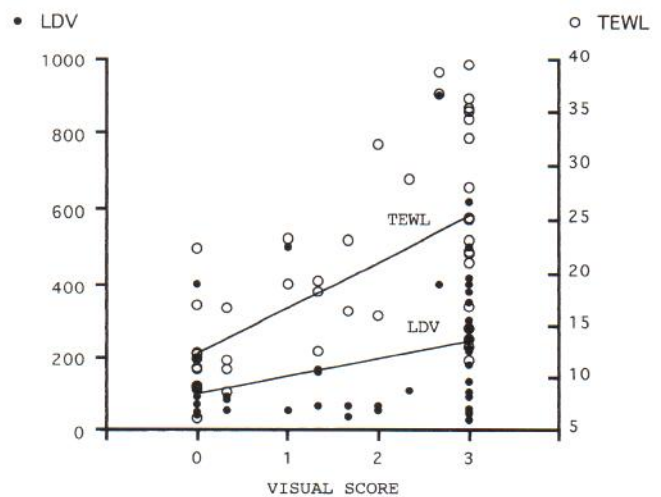


Fig. 1.

constriction must be differentiated from the therapeutic activity of the molecule, which leads to a decreased blood flow after reduction of papillomatosis. At week 3 the therapeutic activity of calcipotriol is comparable to clobetasol in terms of improvement of skin microcirculation. The correlation between visual scoring and instrumental evaluation was significant (Fig. 1), confirming the usefulness of non-invasive techniques in monitoring disease activity in psoriasis.

The study indicates that both treatments were effective, inducing a normalization of visual and bioengineering parameters. In particular, the efficacy of calcipotriol, after 3 weeks of treatment, is comparable to clobetasol, supporting the claim that the use of vitamin analogues in topical long-term treatment of psoriasis minimizes the risks of side-effects induced by potent topical corticoids.

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