

Positive effect of using calcipotriol ointment with narrow-band ultraviolet B phototherapy in psoriatic patients

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Background/purpose: The successful use of narrow-band ultraviolet B (UVB) phototherapy for the management of psoriasis has prompted the examination of various combination treatments with narrow-band UVB. However, there have been contradictory reports on the effect of the calcipotriol–narrow-band UVB combination. This study was performed to compare the clinical efficacy of the calcipotriol–narrow-band UVB combination with narrow-band UVB alone.

Methods: Of the 28 psoriasis patients, 10 were treated with the calcipotriol–narrow-band UVB and 18 with narrow-band UVB alone. Phototherapy was done once daily three times a week and the dose was gradually increased in a stepwise fashion by 0.05 J/cm^2 . At the end of therapy, overall efficacy was classified according to the chosen grading system.

Results: On assessing the therapeutic results using the criteria selected, 90.0% patients ($n=9$) in the calcipotriol–narrow-band UVB group and 61.1% patients ($n=11$) in the narrow-band UVB group showed grade IV at the end of therapy. The calcipotriol–narrow-band UVB group showed more rapid improvement at

the early stage. The final and total UVB dose were slightly lower in the calcipotriol–narrow-band UVB group but no significant difference was observed with respect to the total number of irradiations, duration of treatment, final UVB dose or total cumulative UVB dose required to reach grade IV in both groups ($P>0.05$). The pattern of adverse effects was similar in both groups with a slightly higher frequency in the calcipotriol–narrow-band UVB group.

Conclusion: Our results demonstrated that the total cumulative UVB dose required to reach grade IV was not significantly different in both groups, although it was slightly lower in the calcipotriol–narrow-band UVB group. However, a higher percentage of patients attained grade IV at the end of therapy in the combination group and this therapy was more effective in reducing the Psoriasis Area and Severity Index early in treatment. More studies are warranted to confirm these results.

Key words: calcipotriol; combination; narrow-band UVB.

Phototherapy has been used for the management of moderate to severe psoriasis. Although psoralen ultraviolet A (PUVA) photochemotherapy has been recognized as the most prevalent and effective mode of phototherapy, it is also known to have many limitations. Narrow-band ultraviolet B (UVB) is gaining popularity after it was reported that the most effective UVB wavelength for the treatment of psoriasis is located near 313 nm (1). Recent studies have supported this finding and found that it is superior to broad-band UVB therapy for psoriasis and as effective as the PUVA photochemotherapy (2–4).

It is well established that calcipotriol is a safe and effective

tive treatment for psoriasis (5, 6) and it has been used in combination with various types of phototherapy. Many studies have revealed that the combination of calcipotriol with PUVA leads to a better outcome than phototherapy alone (7, 8); we confirmed these results (9). Bourke et al. reported that the calcipotriol–narrow-band UVB combination had a synergistic effect (10). But Brands et al. concluded that calcipotriol ointment had no synergistic effect when used in combination with low-dose narrow-band UVB phototherapy (11).

Our study was performed to compare the clinical efficacy of calcipotriol–narrow-band UVB combination with narrow-band UVB alone.

Patients and methods

Patients

A total of 28 patients attending the psoriasis clinic at Seoul National University Hospital, Seoul, Korea, were asked to take part in the study. The patients were randomly divided into two groups: 10 were treated with the calcipotriol–narrow-band UVB and 18 with narrow-band UVB alone. Table 1 contains the relevant data concerning age, sex and the initial PASI (Psoriasis Area and Severity Index) of both groups; no significant differences were found between the two groups. Only patients with chronic plaque psoriasis affecting over 5% of the total body surface area were included. Patients with a history of photosensitive disease or cutaneous malignancy, or who had used phototoxic drugs or arsenic were excluded, as were pregnant women and those who had received any kind of systemic treatment or ultraviolet therapy within the previous 4-week period. Following a 4-week washout period, those meeting all of the entry criteria were enrolled.

Methods

Narrow-band UVB source

A Philips TL01/100W fluorescent lamp (Philips, Netherlands), emitting a wavelength of 311 ± 2 nm, was used in a Waldmann 8001k cabinet (Waldmann Co., Villingen-Schwenningen, Germany). Irradiance was measured by a calibrated Waldmann UVB meter. The true dose of narrow-band UVB emission was calculated by multiplying the UVB dose measured by a correction factor derived from the Uvmeter® for TL 01 (Waldmann).

Treatment regimen

Patients received phototherapy once daily three times a week. The initial dosage was set at the lower dose between two values; 1) the 70% of the minimal erythema dose, determined just prior to therapy, and 2) 0.3 J/cm^2 for skin type III or 0.4 J/cm^2 for skin type IV and V. The dose was gradually increased in a stepwise fashion by 0.05 J/cm^2 according to the response of patients and the adverse effects. When the dose at a single session exceeded 1 J/cm^2 , increments were raised by 0.1 J/cm^2 . Treatment was continued until clinical clearance, the occurrence of unacceptable side-effects or when no further improvement oc-

Table 1. Profiles of patients enrolled in narrow-band (NB) UVB and calcipotriol–NB UVB therapy

	NB UVB	Calcipotriol–NB UVB
<i>n</i>	18	10
Age (years; mean \pm SD)*	39.7 ± 14.8	39.7 ± 12.5
Sex (male/female)	7/11	3/7
Initial PASI score*	17.6 ± 12.1	16.3 ± 5.1

* $P > 0.05$.

Table 2. Criteria of response to therapy (12)

Grade	Criteria	Improvement
I	Minimal improvement – slightly less scale and/or erythema	5–20%
II	Definite improvement – partial flattening of all plaques, less scaling and erythema	20–50%
III	Considerable improvement – nearly complete flattening of all plaques, border of plaques still palpable	50–95%
IV	Clearing – complete flattening of plaques may be outlined by pigmentation	> 95%

curred. In the calcipotriol–narrow-band UVB group, calcipotriol ointment $50 \mu\text{g/g}$ (Daivonex, Leo Pharmaceutical Products, Ballerup, Denmark) was applied twice daily, but only after phototherapy.

Patients were not permitted to take other medications, either topically or systemically, that could affect the course of their psoriasis, with the exception of topical treatment in the scalp region.

Clinical assessments

Before therapy, baseline PASI and routine laboratory tests were conducted. PASI and adverse effects were recorded at each visit. At the end of therapy, overall therapeutic efficacy was assessed according to the grading system proposed by the PUVA Cooperative Group of the United States in 1979 (12) (Table 2). We compared the total number of phototherapy sessions, duration of treatments, final UVB dose and total cumulative UVB dose required to reach grade IV in both groups. As the therapeutic response to phototherapy differs according to the location of the psoriatic lesions, the therapeutic effectiveness on the trunk and extremities was evaluated separately.

Statistical analysis

The Mann–Whitney *U*-test was performed to evaluate the differences between the calcipotriol–narrow-band UVB group and the narrow-band UVB group for the trunk and extremities (SPSS® 9.0 version, USA). The Wilcoxon Matched-Pairs Signed-Ranks test was performed to analyse the reduced PASI of both groups. A *P*-value of less than 0.05 was regarded as significant.

Results

Therapeutic efficacy

Before therapy, no significant difference in the PASI of the two groups was found (Table 1). When we assessed the therapeutic results at the end of therapy using the criteria mentioned above, 90.0% patients ($n = 9$) in the calcipotriol–narrow-band UVB group and 61.1% patients ($n = 11$) in the narrow-band UVB group reached grade IV on both trunk and extremities (Table 3). In the narrow-band UVB

Table 3. Results of NBUVB and calcipotriol-NBUVB therapy

	NBUVB	Calcipotriol-NBUVB
Grade IV	61.1% (<i>n</i> = 11)	90.0% (<i>n</i> = 9)
Grade IV at trunk or extremities	16.7% (<i>n</i> = 3)	0.0% (<i>n</i> = 0)
Grade I, II, III	22.2% (<i>n</i> = 4)	10.0% (<i>n</i> = 1)
Total	100% (<i>n</i> = 18)	100% (<i>n</i> = 10)

group, 16.7% patients (*n* = 3) reached grade IV at only one region (trunk or extremity) and a higher percentage of patients failed to attain grade IV. The differences between the number of patients achieving grade IV and those failing to do so in the two groups were significant. Figure 1 shows the change of PASI during treatment. The difference in the PASI reductions of the two groups was significant at week 2 ($P < 0.05$), but this difference was not maintained at weeks 4, 6 and 8.

Therapeutic effectiveness was assessed at the trunk and extremities (Table 4). Although the final UVB dose and the total cumulative UVB dose required to reach grade IV were a little lower in the calcipotriol-narrow-band UVB group, no significant differences were observed in either group ($P > 0.05$).

Side-effects

The most common side-effect was an itching sensation (50.0% in the narrow-band UVB group and 70.0% in the calcipotriol-narrow-band UVB group), but nearly all side-effects were transient and tolerable. Mild to moderate burn also appeared (11.1% in the narrow-band UVB group and 20.0% in the calcipotriol-narrow-band UVB group). In the calcipotriol-narrow-band UVB group, 10.0% of patients (*n* = 1) stopped the treatment because of severe itching sensation; 5.6% of patients (*n* = 1) in the narrow-band UVB group stopped due to burn with vesicle formation.

Discussion

Many studies have reported that narrow-band UVB therapy is more effective than broad-band therapy for the management of psoriasis. Moreover, narrow-band UVB therapy is comparable to PUVA photochemotherapy in terms of its clinical effects and does not require post-treat-

PASI

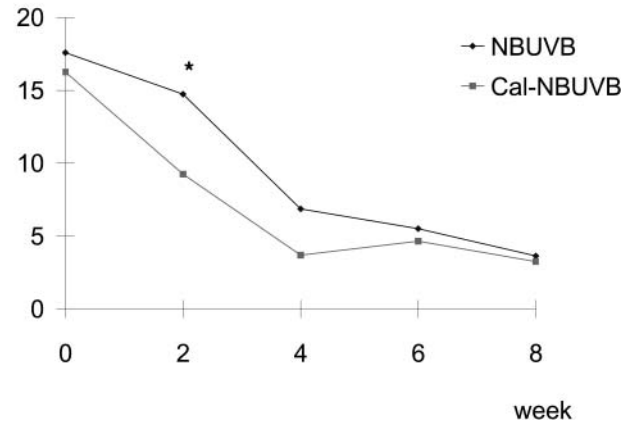


Fig. 1. Change of PASI during the treatment. * $P < 0.05$. PASI: Psoriasis Area and Severity Index. Cal: calcipotriol.

ment eye care or the administration of photosensitizer (4, 13). For these reasons, its use is increasing and various treatments continue to be examined in combination with narrow-band UVB to enhance its clinical effects and reduce side-effects (14–16).

It is known that calcipotriol has an additive effect on PUVA (7–9). But reports are contradictory concerning the combination with narrow-band UVB. Bourke et al. reported that the combined therapy of narrow-band UVB and calcipotriol was significantly more effective in clearing psoriasis than phototherapy alone (10). Brands et al., however, concluded that calcipotriol ointment had no synergistic effect when used in combination with low-dose narrow-band UVB phototherapy (11). They explained that the effect of low-dose narrow-band UVB might overshadow the effect of calcipotriol ointment. In our present study, the use of calcipotriol did not reduce the number of irradiations and total cumulative dose needed to achieve grade IV when used with narrow-band UVB. But there was a tendency for the number of required UVB doses to decrease slightly in the combination group. Another study including more patients may give more detail on this. More patients did reach grade IV in the combination group, and more cases of failure occurred in the narrow-band UVB alone group. In particular, the calcipotriol-narrow-band UVB therapy was more efficient at re-

Table 4. Total number of treatments, duration and NBUVB dose to achieve grade IV at the trunk and extremities

	Trunk NBUVB/Calcipotriol-NBUVB	Extremities NBUVB/Calcipotriol-NBUVB
No. of irradiations	15.7 ± 4.1/14.3 ± 5.8	18.5 ± 4.8/16.0 ± 4.3
Duration of treatment (days)	37.8 ± 13.5/38.3 ± 17.6	43.3 ± 13.9/43.1 ± 13.4
Final dose (mJ/cm ²)	1010.0 ± 183.8/938.9 ± 277.0	1172.7 ± 233.8/1050.0 ± 227.8
Total cumulative dose (mJ/cm ²)	10575.0 ± 3431.0/9922.2 ± 5981.5	14222.7 ± 4789.5/11655.6 ± 4723.0

$P > 0.05$.

ducing the PASI in the early stages. This is desirable in that it can increase patient compliance.

The mean total narrow-band UVB dose of our study was 9.92–14.22 J/cm²; Brands et al. reported a total dose of 36.71–39.88 J/cm². As the UV dose increases, the effect of calcipotriol ointment may be overshadowed. This needs to be confirmed in controlled studies. In this study, calcipotriol was applied only after phototherapy to avoid the blocking effect of UVB (17).

The pattern of side-effects in both groups was similar, although the total incidence was slightly higher in the calcipotriol–narrow-band UVB group. Serious side-effects preventing treatment occurred in only one patient in each group.

In conclusion, our study demonstrated that final UVB dose and total cumulative UVB dose required to reach grade IV were not significantly different in either group, although they were slightly lower in the calcipotriol–NBVB group. However, more patients attained grade IV at the end of therapy in the combination group, and this treatment was more effective in reducing PASI early in the treatment. Based on our results, we feel that calcipotriol ointment may be used as a supplementary agent in the narrow-band UVB phototherapy of psoriatic patients. These results need to be confirmed in studies including more patients.

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