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Calcipotriol vs. tazarotene as combination therapy with narrowband ultraviolet B (311 nm): efficacy in patients with severe psoriasis

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Summary

Background Phototherapy has been shown to be one of the most effective treatment modalities for patients with psoriasis. Nevertheless, photocombination therapies capable both of reducing cumulative ultraviolet (UV) doses and of accelerating clearance of skin lesions are important and of high interest. There have been no published studies comparing the effect of narrowband UVB irradiation in combination with topical application of tazarotene vs. calcipotriol.

Objectives To determine, in a half-side manner, whether a combination of UVB (311 nm) and tazarotene is superior to UVB (311 nm) plus calcipotriol or vice versa.

Methods Ten patients suffering from widespread symmetrical psoriasis were treated for at least 4 weeks with topical calcipotriol and tazarotene in a half-side distribution. Additionally, the whole body was irradiated with narrowband UVB (311 nm) four times a week. Before treatment and once weekly during therapy a modified Psoriasis Area and Severity Index was estimated for each body half. The total treatment time, number of treatment sessions and cumulative UVB dose necessary for clearance of skin lesions were determined in an observer-blind fashion for each patient. Furthermore, all patients completed a quality of life questionnaire.

Results Clearance of psoriasis was observed after a median of 19 treatment sessions (range 14–28) and a median cumulative UVB dose of 22·98 J cm^{-2} (range 9·24–58·22) simultaneously for both body halves. On the side treated with topical tazarotene gel, four patients complained of itching and dryness of the skin, and skin irritation was observed in three of them. Six patients preferred the application of tazarotene gel, while four preferred calcipotriol.

Conclusions Our clinical comparison of narrowband UVB with either topical calcipotriol or topical tazarotene revealed no significant therapeutic difference between both regimens. Although these results need to be confirmed in larger patient groups, we feel that both photocombination therapies can broaden the therapeutic options for moderate to severe psoriasis vulgaris and may reduce the cumulative UVB dose during therapy.

Key words: calcipotriol, narrowband ultraviolet B, phototherapy, psoriasis, tazarotene

A recent advance in phototherapy of psoriasis has been the introduction of narrowband ultraviolet (UV) B using a fluorescence irradiation device delivering virtually monochromatic light at 311 nm. Phototherapy with narrowband UVB is today considered to be one of the most effective treatment modalities for patients with psoriasis while offering an excellent short-term benefit/risk ratio. An improved efficacy and therapeutic index of narrowband UVB in comparison with conventional broadband UVB irradiation has been shown in many studies.[1–4] Furthermore, some studies have documented a longer remission period after narrowband UVB (311 nm) compared with broadband UVB.[2] However, long-term side-effects of this treatment modality remain to be assessed thoroughly. Therefore, photocombination therapies capable of both reducing cumulative UVB doses and accelerating resolution of skin lesions are important and of high interest.

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Combining narrowband UVB with calcipotriol, a vitamin D_3 analogue, is considered a very effective treatment for psoriasis, offering a clinical efficacy comparable with psoralen plus UVA therapy.[5] It has recently been shown that combination of narrowband UVB with tazarotene, the first member of a novel class of topical acetylenic retinoids, also enhances the therapeutic efficacy of the UV irradiation, with reduction of the mean number of treatment sessions and the cumulative UVB dose.[6] Furthermore, the major limitation of tazarotene monotherapy, induction of skin irritation, was markedly reduced using the photocombination regimen, possibly due to an enhanced skin barrier.[6] However, there are no published studies comparing the efficacy of narrowband UVB plus topical tazarotene vs. its combination with topical calcipotriol application.

Patients and methods

Ten patients suffering from widespread symmetrical psoriasis were included in our comparative treatment study. Enrolment excluded patients with erythrodermic or pustular psoriasis. Before treatment a medical history was obtained, and each patient received a thorough physical examination, which included a clinical assessment of psoriasis using the Psoriasis Area and Severity Index (PASI) score. Of the six men and four women with a mean age of 53 years (range 23–62), seven patients suffered from plaque-type psoriasis and three from guttate psoriasis. According to the classification of Fitzpatrick,[7] six patients had skin phototype II, two patients had skin phototype III and two patients had skin phototype I.

Psoriatic lesions on each side of the body were treated with either topical tazarotene gel 0·05% or calcipotriol ointment (0·05 mg g^{-1}) once daily, with random assignment of topical treatment to body halves. The patients were instructed to apply a thin film of tazarotene gel or calcipotriol ointment to all psoriatic lesions of one body half each evening.

In addition to topical treatment, narrowband UVB (311 nm) irradiation of the whole body was performed once daily, four times a week. The irradiation was performed using 26 Philips TL-01/100 fluorescent bulbs mounted in a UV 1000 cabin (Waldmann, Villingen-Schwenningen, Germany). The bulbs in this device were evenly distributed throughout 360° and emitted narrowband UVB radiation with an average intensity of 13·4 mW cm^{-2} as measured with a calibrated UV meter (Waldmann) at a distance of 20 cm. Depending on the individual skin phototype, the initial UVB doses ranged from 0·14 to 0·32 J cm^{-2}, with doses gradually increasing up to a maximum of 295 J cm^{-2} according to the criteria listed in Table 1.

Table 1. Initial dose and increments of ultraviolet B (311 nm) irradiation dosage

Initial dose	0·14–0·32 J cm^{-2}
No erythema	+0·14 J cm^{-2}
Slight erythema	No increase
Moderate erythema	−0·14 J cm^{-2}
Marked erythema or burning	No irradiation

Before treatment and once weekly during the treatment an observer-blind modified PASI was determined for each body side.[8] Furthermore, the total treatment period, number of treatment sessions and cumulative UVB dose necessary for the clearance of the skin disease were documented for each patient, and all patients completed a quality of life questionnaire evaluating which of the topical treatments used they would prefer in the future if another therapy course became necessary (and the reasons for this preference).

Non-parametric tests for small samples at the 0·05 significance level were used for statistical evaluation. To compare the therapeutic effectiveness of both therapy regimens the Wilcoxon-signed rank sum test, a one-sample test, was chosen.

Results

The median PASI score at baseline was 13·5 [95% confidence interval (CI) 9·47–17·22, range 9·4–20]. Both treatment modalities (narrowband UVB plus calcipotriol and narrowband UVB plus tazarotene) notably reduced the PASI scores during therapy, with no clinically significant difference. After 4 weeks the median PASI score for the body half assigned to UVB plus tazarotene had decreased to 7·0 (95% CI 2·18–10·61) vs. a decrease to 6·0 (95% CI 2·83–9·10) for the body half assigned to UVB plus calcipotriol (Fig. 1).

Complete clearance of the skin disease was observed after a median of 19 treatment sessions (range 14–28) and a median cumulative UVB dose of 22·98 J cm^{-2} (range 9·24–58·22) for both body sides. Statistical analysis of all results revealed no significant difference in the reduction of the PASI scores between UVB plus calcipotriol and UVB plus tazarotene at any time point.

On the side of the body treated topically with tazarotene gel, four patients complained of itching and dryness of the skin. In these four patients, there

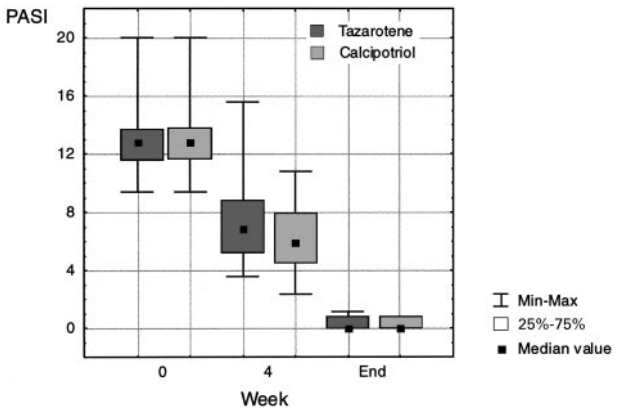

Figure 1. Photocombination therapy of narrowband ultraviolet (UV) B (311 nm) with tazarotene gel vs. narrowband UVB (311 nm) with calcipotriol: Psoriasis Area and Severity Index (PASI) scores during therapy.

was a mild skin irritation observed in two cases and one patient withdrew from treatment due to moderate local irritation. On the body half treated with calcipotriol we observed hyperpigmentation strictly limited to the area of application of the ointment in one patient.

The questionnaire revealed that six patients would prefer tazarotene and four patients calcipotriol if another course of topical treatment were necessary. The patients preferring tazarotene specified that the aqueous formulation of tazarotene was easier to apply and that the calcipotriol ointment, on the other hand, was too greasy and sticky. However, the other four patients specifically preferred the characteristics of the calcipotriol formulation and complained about skin irritation caused by tazarotene gel.

Discussion

No significant therapeutic difference was detected between narrowband UVB (311 nm) in combination with topical calcipotriol vs. combination with tazarotene gel as assessed in a half-sided manner. Clearing of psoriasis was reached with both regimens within the same period of time and with identical cumulative UVB doses. In some cases clinical improvement seemed to begin slightly sooner in the body half treated with tazarotene gel, but from the third week of treatment both sides generally showed identical responses.

In our study, both calcipotriol and tazarotene were applied only once daily. When administering calcipotriol as monotherapy for psoriasis vulgaris it is often applied twice a day, which may well achieve a better therapeutic response than a once-daily application. However, we felt that in combination with phototherapy, a second application of the ointment per day would not result in a better therapeutic result and would considerably restrict the patient's daily life and demand a high degree of compliance; therefore, we decided to test the more realistic once-daily application of topical calcipotriol against the once-daily application of tazarotene, which might have biased the treatment outcomes slightly in favour of tazarotene.

Calcipotriol was generally very well tolerated, although in one patient we observed hyperpigmentation strictly limited to the area to which the agent was applied, as described by Glaser *et al.*[9] The major limitation of tazarotene monotherapy is probably the induction of skin irritation observed in 23% of patients treated with this regimen.[10] We observed local irritation in the body half assigned to tazarotene in three patients, but it was usually not as severe as seen in unirradiated skin. This might be explained by the observation that UVA- and UVB-irradiated skin is more resistant to irritants such as sodium lauryl sulphate than unirradiated skin, because of an enhanced skin barrier.[11] However, one of our patients had to withdraw from topical therapy with tazarotene due to moderate irritation after failure to apply the gel strictly to psoriatic lesions (despite our recommendations). This underlines the importance of thorough counselling and high compliance of the patient when prescribing topical tazarotene gel. Nevertheless, our questionnaire revealed that six patients preferred the aqueous tazarotene gel over the calcipotriol ointment, due to its more pleasant formulation. Another possible advantage of tazarotene might be the anticarcinogenetic potential of topical retinoids, especially in the light of the as yet undefined carcinogenic risk of long-term narrowband UVB irradiation.

Based on our preliminary results, we propose that both the combination of narrowband UVB phototherapy with calcipotriol as well as with tazarotene should be included as first-line treatments in the menu of choices of photocombination therapies for treating moderate to severe psoriasis. These pilot results need to be confirmed in multicentre studies investigating larger patient groups.

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