Narrowband UV-B Phototherapy vs Photochemotherapy in the Treatment of Chronic Plaque-Type Psoriasis

A Paired Comparison Study

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Objective: To compare the therapeutic efficacy of narrowband (TL-01) UV-B phototherapy vs photochemotherapy (psoralen–UV-A [PUVA]) in patients with chronic plaque-type psoriasis.

Design: Open, nonrandomized, intraindividually controlled paired comparison study.

Setting: Phototherapeutic unit in a university hospital.

Patients: Twenty-five patients with chronic plaque-type psoriasis.

Interventions: Paired irradiations with threshold erythemogenic doses of narrowband UV-B and PUVA were given to the patients’ dorsal aspect including the arms and legs. Treatment was performed 3 times weekly until complete or almost complete clearing with one or both regimens or over a maximum period of 18 exposures.

Main Outcome Measures: Assessment of the Psoriasis Area and Severity Index (PASI) in each half of the patient’s dorsal aspect before and after treatment with the 2 regimens.

Results: The median pretreatment PASI score of 16 (range, 6.2–23.4) was reduced by 84% to 2.5 (range, 0.0–12.6) by the narrowband UV-B treatment and by 89% to 1.8 (range, 0.0–8.2) by the PUVA treatment. Statistical analysis of these data showed a tendency for PUVA being superior to narrowband UV-B although the difference remained below the level of significance ($P = .17$). However, a clear effect of the pretreatment PASI score on the therapeutic outcome was found. Patients with higher baseline PASI scores responded significantly better to PUVA than to narrowband UV-B ($P = .03$).

Conclusions: Our data demonstrate that in many patients with plaque-type psoriasis, narrowband UV-B is comparably as effective as PUVA and, given the lack of photosensitizer-related adverse reactions and the possibly lower long-term cancer risk, can be considered as first-line treatment. Treatment with PUVA, on the other hand, remains the mainstay for patients with high PASI scores who do not respond or whose psoriasis cannot be controlled adequately by narrowband UV-B.

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Conventional phototherapy with broadband UV-B and photochemotherapy (psoralen–UV-A [PUVA]) are very efficient and widely used treatment modalities for psoriasis. The choice of treatment depends on the type and severity of psoriasis, the patient’s age and general health, and the consideration of treatment-associated long-term risks. Comparative studies have shown that PUVA is therapeutically more effective than broadband UV-B radiation. Conversely, treatment with UV-B is much easier to perform, requires less precautions to prevent acute adverse reactions, and seems to harbor a considerably lower carcinogenic potential than PUVA. Based on these differences, broadband UV-B phototherapy is primarily indicated in patients with mild to moderate psoriasis, whereas for severe forms of PUVA is indicated.

For editorial comment see page 589

This rough distinction between the use of phototherapy and PUVA for psoriasis had to be reevaluated when in the early 1980s a fluorescent lamp emitting narrowband UV-B between 311 and 313 nm (referred to as the TL-01 lamp) was developed by Philips to improve the efficacy of phototherapy. The rationale for manufacturing such a lamp was derived from action spectra studies for the phototherapy of psoriasis in which longer wavelengths in the UV-B region were indicated to have the best ratio of antipso-
PATIENTS AND METHODS

Twenty-five patients with skin type II or III who consented to participate after having received full information on the setup and the purpose of the trial were consecutively enrolled in this open paired-comparison study. All of these patients had generalized, chronic plaque-type psoriasis in a largely symmetrical distribution and had not received any specific antipsoriatic treatment within the last 4 weeks prior to the study. At the beginning and at the end of the study the Psorias Area and Severity Index (PASI) score was determined separately for each half of the patient’s dorsal aspect (hereafter, half-side).

HALF-SIDE TREATMENT

The PUVA treatment was performed with a liquid preparation of 8-methoxypsoralen (methoxsalen) (Oxsoralen; Gerot Pharmazeutika, Vienna, Austria) at a dosage of 0.6 mg/kg. Prior to the initiation of the half-side comparison first the minimal erythema dose of narrowband UV-B (MEDTL-01) and subsequently the minimal phototoxic dose (MPD) were determined in each patient. Treatment was given 3 times weekly on Monday, Wednesday, and Friday in an irradiation unit for supine therapy. No additional specific systemic or local antipsoriatic therapy was given; however, the patients were allowed to apply emollients after the treatments.

To reduce the patient’s additional expenditure on time, the half-side comparison was performed only on the dorsal side of the whole body that included the dorsal aspect of the arms and legs. On each treatment day the patient first received the narrowband UV-B irradiation on the right side of the dorsal aspect. During the irradiation the rest of the body was covered by 4 layers of white, tightly woven cotton that completely prevented the transmission of UV light. Immediately after the UV-B exposure, the patients ingested the psoralen capsules. One hour later, the left side of the patient’s dorsal aspect and subsequently the whole ventral aspect were exposed to UV-A, while the body area previously treated with narrowband UV-B was shielded from receiving additional UV-A radiation. The initial irradiation dose was 1 MEDTL-01 and 1 MPD. Patients with a negative MPD test were treated with a skin type–based initial UV-A dose of 1 J/cm² for skin type II and 2 J/cm² for skin type III. Subsequent dose adjustments were based on the patient’s history and the clinical examination and aimed at eliciting or maintaining a slight erythematous reaction with both treatments. The irradiation dose was unaltered when the patients reported or still had erythema and was increased by 20% in skin type III and by 10% in skin type II patients, respectively, in the absence of an erythematous response. Owing to the different time courses of phototesting and treatment with narrowband UV-B was done with a Waldmann UV 3003 lay down irradiation unit (Waldmann; Werk für Lichttechnik, Schwenningen, Germany) equipped with 15 Philips TL 100W/01 fluorescent tubes. The MEDTL-01 was determined by exposing the patient’s buttocks to a geometrical dose range between 141 and 566 mJ/cm². The irradiance at skin level was, on average, 3.85 mW/cm² and measured with an IL 1700 research radiometer (International Light, Newburyport, Mass) and NS 313–filtered SD 240 probe with a spectral response from 308 to 318 nm (half-power points) and a peak sensitivity at 313 nm.

Subsequent to the MEDTL-01 testing, the MPD was assessed with a Waldmann PUVA 500 irradiation unit equipped with 10 Philips TLK 40W/09N UV-A lamps. The irradiance at skin level was 10.5 mW/cm² as measured with a Waldmann UV meter whose spectral sensitivity corresponds to the spectral emission of the UV-A lamps. The UV-A dose range was 0.5 to 5 J/cm² for skin types I or II and 1.5 to 9 J/cm² for skin types III or IV. A Waldmann PUVA 4000 lay down unit equipped with 40 Sylvania FR 90 T 12 / PUVA fluorescent tubes was used for the therapeutic irradiations. The irradiance was on average 12.6 mW/cm² as measured by an integrated radiometer.

STATISTICAL METHODS

Within the framework of a hierarchical model an analysis of covariance was performed using the GLM program of SAS. Thus, the possible effect of the baseline PASI score, the treatment, and the interaction between the baseline PASI score and treatment were analyzed taking into account the block structure of the study (each patient receiving both treatments).
They observed a 100% success rate in the etretinate-PUVA group as opposed to a 93% success rate in the etretinate-narrowband UV-B group and an 80% success rate in the narrowband UV-B monotherapy group. A direct comparison between narrowband UV-B and PUVA was not included in that study.

The present investigation was undertaken to evaluate on a larger scale the therapeutic potential of narrowband UV-B phototherapy in relation to PUVA and to determine whether in patients with moderate to severe chronic plaque-type psoriasis, narrowband UV-B phototherapy may serve as an effective therapeutic alternative to PUVA.

RESULTS

All patients completed the study. Of these, 21 patients consistently had a comparable number of erythrogenic events with both treatments during the study period, whereas in 4 patients the PUVA-induced erythema occurred only after 8 to 13 exposures and on fewer occasions than with narrowband UV-B. Since it was the aim of the study to compare the therapeutic efficacy of equierythrogenic dosages, these latter 4 patients were excluded from evaluation. The remaining 21 patients were of skin types II (7 patients) or III (14 patients), with a median duration of psoriasis of 17 years (range, 1-46 years). In all these patients, the MEDTL-01 was within the range of test doses with a median of 400 mJ/cm² (range, 141-566 mJ/cm²). The MPD test gave a negative result in 3 of the 21 patients. The median MPD of the remaining 18 patients was 1.5 J/cm² (range, 0.5-5 J/cm²).

The treatment results summarized in Figure 1 show the PASI score of each patient at baseline and after treatment with PUVA and narrowband UV-B, respectively. There was a significantly better response to psoralen–UV-A than to narrowband UV-B with increasing baseline score (P = .03 by covariance analysis).

![Figure 1](http://archderm.jamanetwork.com/pdfaccess.ashx?url=/data/journals/derm/11686/)

**Figure 1.** The Psoriasis Area and Severity Index scores of all patients arranged in order of increasing magnitude before and after treatment with narrowband UV-B and psoralen–UV-A. There was a significantly better response to psoralen–UV-A than to narrowband UV-B with increasing baseline score (P = .03 by covariance analysis).

<table>
<thead>
<tr>
<th>Initial UV Dose, J/cm²</th>
<th>Final UV Dose, J/cm²</th>
<th>Total UV Dose, J/cm²</th>
<th>No. of Exposures</th>
<th>Treatment Duration, d</th>
<th>PASI† Score</th>
</tr>
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<tbody>
<tr>
<td></td>
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<td></td>
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<td></td>
<td>Baseline</td>
</tr>
<tr>
<td>Narrowband UV-B</td>
<td>0.4 (0.14-0.57)</td>
<td>1.42 (0.48-2.45)</td>
<td>12.7 (1.8-22.3)</td>
<td>15 (6-18)</td>
<td>38 (18-53)</td>
</tr>
<tr>
<td>Psoralen–UV-A</td>
<td>1.5 (0.5-5.0)</td>
<td>3.1 (0.9-8.6)</td>
<td>40.1 (6.9-87.5)</td>
<td>15 (6-18)</td>
<td>38 (18-53)</td>
</tr>
</tbody>
</table>

*Values are medians (ranges).
†PASI indicates Psoriasis Area and Severity Index.
‡P = .17 by analysis of covariance.

The treatment results summarized in Figure 1 show the PASI score of each patient at baseline and after treatment with PUVA and narrowband UV-B, respectively. The overall response to PUVA was slightly superior to narrowband UV-B phototherapy. After a median of 15 exposures (range, 6-18 exposures) and 38 days (range, 18-53 days), the median baseline PASI score of 16 (range, 6.2-23.4) was reduced by 84% to 2.5 (range, 0.5-12.6) by the narrowband UV-B treatment and by 89% to 1.8 (range, 0-8.2) by the PUVA treatment (Table). The median cumulative doses of narrowband UV-B and UV-A were 12.7 J/cm² (range, 1.8-22.3 J/cm²) and 40.1 J/cm² (range, 6.9-87.5 J/cm²), respectively. By analysis of covariance, no significant difference was found in the overall efficacy of the 2 regimens (P = 0.17).
However, when the patients were stratified according to their pretreatment PASI score the correlation to treatment response was significant. With increasing PASI scores the patients’ psoriasis cleared better with PUVA than with narrowband UV-B phototherapy ($P = .03$) (Figure 1).

In the direct left to right comparison, 4 patients showed a better response to narrowband UV-B, 6 responded equally to both treatments (Figure 2), and 11 had a greater degree of clearing with PUVA (Figure 3). The half-side differences were, however, slight in most patients. Complete or almost complete clearing was induced on the dorsal half-side by PUVA in 9 patients and by narrowband UV-B in 7, respectively (2-tailed $p = 0.75$ by Fisher exact test).

Irrespective of the treatment modality, a higher reduction of the PASI score ($P < .001$) and a higher probability to clear completely within the study period ($P = .03$) was found for patients with lower pretreatment PASI scores.

Only few and minor side effects occurred during the study period. In the initial phase of treatment, 3 patients experienced moderate nausea after the ingestion of the psoralen capsules which, however, did not necessitate any specific antiemetic treatment and subsided spontaneously during the later course of treatment. One patient reported itching in both the narrowband UV-B– and PUVA-treated skin areas. Another patient developed lesional blistering $^{24}$ on the right side of her back after 14 irradiations with narrowband UV-B.

The development of the TL-01 lamp with a higher therapeutic potential than conventional broadband UV-B sources as well as the increasing awareness of the carcinogenic risk associated with long-term PUVA $^{6,7}$ have led to a continuously growing use of narrowband UV-B phototherapy in psoriasis. With regard to the relative therapeutic effectiveness of narrowband UV-B and PUVA, however, only sparse data are available. $^{20,21}$ Such information is particularly important for patients with moderate to severe chronic plaque-type psoriasis as, besides the palmoplantar and the rare erythrodermic and pustular forms of psoriasis, it is this type of psoriasis where PUVA is primarily indicated.

The only half-side comparison study on narrowband UV-B vs PUVA conducted so far was published by van Weelden et al $^{20}$ in 1990. They treated 10 patients with widespread psoriasis vulgaris twice weekly with slightly erythematous dosages over a maximum period of 4 weeks. Within the relatively short study period “on average no significant difference was found between the overall therapeutic effectiveness of narrowband UV-B and PUVA.” However, the therapeutic result differed depending on the body site. Whereas the lesions on the trunk responded better to narrowband UV-B the opposite was true for the psoriatic plaques on the arms.
and legs. These findings indicated that PUVA might be more effective for lesions that are more recalcitrant to therapy.

In our study treatment was given thrice weekly over a maximum period of 18 exposures. To apply bioequivalent doses of both irradiations, we followed a slightly erythemogenic dosimetry as was done in the trial by van Weelden et al. 20 The overall improvement, ie, the reduction of the median pretreatment PASI score, did not differ significantly between the 2 regimens. However, a positive correlation between the magnitude of the baseline PASI score and the probability to clear better with PUVA treatment was found indicating that in patients with high PASI scores, PUVA is more likely to induce complete or almost complete remission.

Taken together, our data demonstrate that in many patients, in particular those with moderate or moderate to severe psoriasis, narrowband UV-B is comparably as effective as PUVA whereas in the more severely affected, PUVA is superior. This is in agreement with previous studies that by retrospective or direct comparison found a similar efficacy of narrowband UV-B relative to PUVA in psoriasis 19,20 but also revealed that in a subset of patients treatment with PUVA is required to achieve a satisfactory response. 21

The use of narrowband UV-B offers some major advantages owing to the fact that it does not depend on the concomitant administration of a photosensitizer. In oral PUVA psoralen intolerance reactions, the variability of the psoralen levels, hepatic diseases, and drug interactions have to be taken into account. In addition, the systemic photosensitization necessitates adequate eye protection and prolonged sun avoidance. With bath PUVA many of these disadvantages are obviated; however, the requirement of the bathing procedure limits the broader use of this treatment modality.

Controversial data are found in the literature on the incidence and severity of burning reactions under narrowband UV-B treatment. Compared with broadband UV-B, both a lower 11,17 as well as a higher frequency 20 of burning episodes or more intense erythematous reactions 19 were reported. Differences in the irradiation protocol and the patient’s skin type seem to be important in this regard. In our study, none of the patients experienced a severe burning episode with either one of the 2 regimens.

The consideration of treatment-associated long-term risks, in particular the carcinogenic potential, is a central issue in the choice of treatment for patients with psoriasis. The assessment of cancer risk resulting from the clinical use of narrowband UV-B is based on retrospective studies on broadband UV-B–treated patients 6,7,27,28 and on mouse studies comparing the carcinogenicity of broadband vs narrowband UV-B. 15,29,30 These data suggest that the cancer risk of equitherapeutic doses of narrowband UV-B is not greater than that of broadband UV-B and substantially lower than that of PUVA. 15,31 This assumption has recently gained further support from an in vitro study indicating that phototherapy with narrowband UV-B does not produce more DNA damage than treatment with broadband UV-B. 31

Considering the good therapeutic efficacy and the low profile of acute and possibly also long-term side effects, we consider narrowband UV-B as first-line treatment for patients with moderate to severe plaque-type psoriasis. Psoralen–UV-A on the other hand, remains the mainstay for patients with severe psoriasis whose conditions do not respond or cannot be controlled adequately by narrowband UV-B. The optimum treatment protocol for narrowband UV-B and, in particular, the average duration of remission are yet to be determined in larger patient cohorts. 35 In addition, prospective follow-up studies are required to assess the long-term risks in humans associated with therapeutic exposures to narrowband UV-B radiation.

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REFERENCES


