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Comparison of Narrow-band UV-B Phototherapy and PUVA Photochemotherapy in the Treatment of Psoriasis

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The therapeutic effectiveness of a new fluorescent lamp, Philips TL-01, which emits a narrow peak around 311–312 nm, was compared with the currently used PUVA photochemotherapy consisting of oral 8-MOP followed 2 h later by UV-A from fluorescent lamps Philips TL-09. Comparisons of therapeutic efficacy were performed in 10 patients with widespread, symmetrically distributed psoriasis lesions. They received treatment with PUVA on one half of the body and with TL-01 light on the other half; both treatments were given twice a week. It is concluded that on the average phototherapy with narrow-band UV-B is an effective as PUVA; it is certainly more convenient and probably less carcinogenic.

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Therapies in which ultraviolet radiation is used are based on the experience of psoriatic patients, that sunlight has a beneficial effect. Part of the therapies evolved may be classified as those which use a photosensitizer (1, 2), and more recently PUVA photochemotherapy (3, 4). With regard to the therapies without the use of a photosensitizer, several investigators have reported the influence of wavelength on the therapeutic efficacy. Fischer (5) found 313 nm more effective than longer wavelengths, in the UV-A region. In fact, investigations by Young et al., Parrish, and van Weelden et al. (6, 7, 8) showed that UV-A with wavelengths longer than 315 nm is practically ineffective.

The UV-C wavelengths, below 280 nm, are also relatively ineffective (8, 9). Consequently, the most effective wavelengths are between 280 and 313 nm. Especially the longer wavelengths in this region are the most effective (9, 10, 11).

More recently van Weelden et al. (12, 13) investigated the possibility to improve the effectiveness of phototherapy by using a light source emitting radiation restricted to these longer wavelengths in the UV-B region. By the method of paired comparisons, the therapeutic effectiveness of a new narrow-band UV-B fluorescent lamp, Philips TL-01, which emits a narrow peak around 311–312 nm, was compared with the currently used Philips TL-12, which emits a broad spectrum around 280–350 nm with a peak near 305 nm. It was concluded that the improvement of the skin condition obtained with the TL-01 lamp was superior to that of the TL-12 lamp. In mice the TL-01 light was also less carcinogenic than the TL-12 light (13). The clinical advantages of the narrow-band UV-B lamp over the currently used broad-band UV-B lamp were confirmed by Green et al., Karvonen et al. and Larkö (14, 15, 16).

In a previous study by van Weelden et al. (8) it was concluded that on average broad-band UV-B Westinghouse sunlamps are as effective as PUVA, while sometimes preferences were observed for one of the two forms of therapy in individual patients.

To conclude from these studies (8, 13) that in psoriasis the narrow-band UV-B lamp is more effective than PUVA would be presumptuous and incorrect. It was therefore decided to compare directly the effectiveness of narrow-band UV-B phototherapy and the currently used PUVA photochemotherapy.

MATERIALS AND METHODS

Ten patients, 8 male and 2 female (age range 21–73 years, mean 48) with widespread symmetrical psoriasis vulgaris participated in this study. The duration of the disease ranged between 1 and 63 years (mean 22 years). The patients were hospitalized throughout the investigation.

The patients were exposed to UV radiation from fluorescent light tubes in two different square light cabinets with reflecting walls. In this study the first cabinet (8), measuring $1\,^1/_2 \times 1\,^1/_2$ m, contained 94 40-W and 144 20-W lamps of type

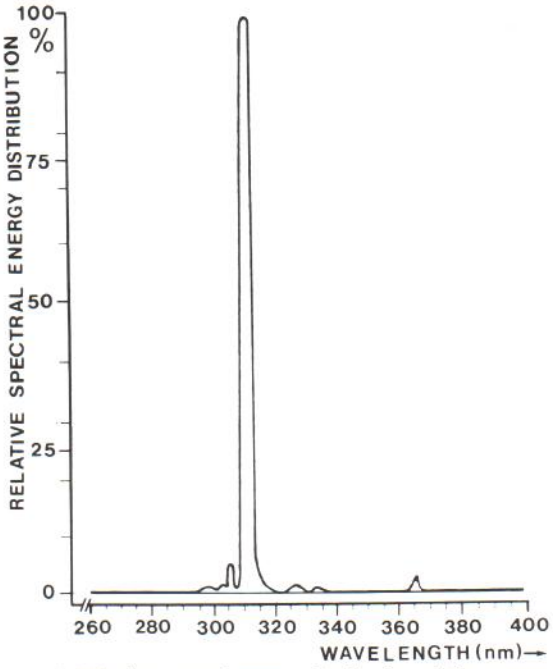

Fig. 1. Relative spectral energy distribution of the narrow band UV-B fluorescent lamp, Philips TL-01.

Philips TL-09. These lamps emit mainly UV-A and are of the same type as used in many cabinets for PUVA therapy. The second cabinet (13), measuring 1.30×1.30 m, contained 64 40-W en 64 20-W narrow-band UV-B lamps of type Philips TL-01.

As in previous experiments (8, 13), 1% salicylic acid in petrolatum was applied daily to the entire skin of all patients, in order to remove psoriatic scales and to prevent dryness of the skin, which is known to be a common effect of regular exposures to UV radiation. The ointment was always applied after the exposures, so it was not likely to influence the effect of the radiation.

Light sources and irradiance measurements

The lamps used for PUVA therapy, Philips TL-09, emit mainly UV-A and less than 0.5% UV-B. The spectrum of the new narrow-band UV-B lamps used in this study, Philips TL-01, is dominated by a strong and narrow peak (bandwidth 2.5 nm) around 311–312 nm, with a second peak around 305 nm (Fig. 1). Compared with the currently used fluorescent UV-B lamps, such as Philips TL-12 and Westinghouse FS sunlamps, the TL-01 has a much smaller output at the most erythematogenically effective wavelengths of 300 nm and below.

The relative spectral distribution measurements were performed with a monochromator (Jarrell-Ash, model 84–425 SP), bandwidth 1.2 nm, in combination with a photomultiplier (Hamamatsu R212).

The irradiance in the two light cabinets as used in the therapies compared was measured over the full spectral range with a calibrated Kipp thermopile, type E11 (Kipp, Delft, The Netherlands). The irradiances were checked routinely with a Waldmann UV-A or UV-B detector (Waldmann AG, Schwenningen, FRG). The detectors were placed at the level of the patient's trunk. The irradiance in the 'PUVA cabinet' was on average 5.6 mW/cm^2 and in the UVB cabinet, 2.2 mW/cm^2.

Dosimetry; therapeutic effectiveness

The PUVA photochemotherapy was compared with the narrow-band UV-B phototherapy by the method of paired comparison (17, 18). The patients received treatment with narrow-band UV-B on one half of the body and with PUVA on the other half. The side not being treated was shielded by an overall cut in half lengthwise. At the beginning of the comparisons in a patient the treatments were assigned randomly to the two halves of the body, and that assignment was kept the same throughout the investigation. Both treatments were given twice a week.

The UV-B doses were chosen with the aim of eliciting a slight erythema after each exposure (8). The first exposure was 70% of the predetermined minimal erythema dose (MED) on the trunk. The successive doses were given on the basis of the rule that, if the previous exposure had caused no perceptible effect, the next exposure time was increased by 40%; if the previous exposure induced just a slight erythema the next exposure time was increased by 20%; in case of marked erythema, the same exposure time was used again.

The day after the UV-B exposure to one half of the body, PUVA was administered to the other half. The oral dose of 8-methoxy psoralen (8-MOP) was 0.6 mg/kg body weight. The UV-A radiation was given 2 h after the intake of the 8-MOP (Meladinine®, Boehringer Ingelheim). The doses of UV-A were again chosen according to the guideline of causing a slight erythema after each exposure. The first exposure given was 70% of the predetermined MPD. The subsequent exposures were given on the basis of the skin reactions; if the previous exposure had caused no noticeable effect, the next exposure time was increased by 40%; if the previous exposure induced a doubtful erythema it was increased by 20%; and if it caused a slight erythema, the same exposure time was used again. This practice was slightly different from that with UV-B; this was because 1 MPD exposure takes 3 days to develop, whereas a 1 MED UV-B exposure develops within one day.

The therapeutic effects were assessed regularly by experienced clinical observers who had no knowledge of which therapy was given to which side of the patient. From a previous study (8) we knew that cross-over effects did not play an important role in experiments of this type. On the basis of a semiquantitative scoring (0–3+) of erythema, scaling and infiltration, the observers recorded which side was better, or that there was no difference. The observers recorded not only the therapeutic effects on the two sides of the patient's skin as a whole, but also differentiated the comparisons on the trunk, the arms and the legs.

RESULTS

The mean minimal erythema dose (MED) (±SE) before therapy was 400±40 mJ/cm^2 for narrow-band UV-B and the mean minimal phototoxic dose (MPD) (±SE) before therapy was 1.95± 0.34 J/cm^2 of UV-A for PUVA. The treatments started based

Table I. *Comparison of therapeutic effectiveness of TL-01 and PUVA in 10 patients with psoriasis*

	Therapeutic effectiveness on		
	Trunk	Arms/ legs[a]	Overall impression
TL-01 better	4	2	2
'No difference'	4	3	5
PUVA better	2	4	3

[a] In one patient, no comparisons were made on arms and legs.

on these initial MEDs and MPDs and were continued until the comparisons of the symmetrical body sides gave the same difference two times in a row. The conclusion 'no difference' was not drawn before a period of 4 weeks of treatment had been completed. The results of the comparisons are shown in Table I. The assessments by the clinical observers were always in good agreement.

narrow-band UV-B phototherapy and PUVA photochemotherapy. In individual cases, narrow-band UV-B could be better than PUVA on the trunk, but not so on arms or legs, or even the converse. Such an observation in a patient could result in the overall impression 'no difference'. Overall impression was the major criterion in this study. In 3 cases, PUVA gave a better result than narrow band UV-B, in 2 cases narrow-band UV-B was better than PUVA, and in the remaining 5 cases there was no difference. Thus, on average no significant difference was found between the overall therapeutic effectiveness of narrow-band UV-B and PUVA [Sign test and Wilcoxon test (19)].

After completion of the comparisons in a patient, treatment with the therapy which gave the best therapeutic result was applied in principle to the whole body. The choice of the 'best' therapy was made in consultation with the patient. Only 3 patients preferred whole-body treatment with PUVA. This was in accordance with the overall impression of the observers. In the remaining 7 patients the choice of the ultimate therapy for the whole body was narrow-band UV-B; these were the patients where TL-01 light had given results equal to or better than PUVA.

After the patients had cleared or improved to a satisfactory level, the treatment was discontinued. As in the two previous studies (8, 13) no maintenance therapy was given.

DISCUSSION

In the present study, phototherapy with the narrow-band UV-B fluorescent lamps was on average as effective as PUVA. However, in individual patients the assessments of the observers indicated that one of the two therapies was preferable.

The method of paired comparison automatically eliminates the differences between patients and allows us to test the differences between the two therapies more directly. By aiming at a slight erythema after each exposure, the two therapies are given equal chances. This results in a comparison with a strong conclusive force and, therefore, large numbers of patients are not required.

On the trunk, narrow-band UV-B gave a better result in 4 patients and in 2 patients PUVA was better. On the arms and legs, however, it was just the other way round. The trunk is the most sensitive part of the body. Using the guideline of aiming at a slight erythema after each exposure, the successive doses are therefore predominantly determined by the sensitivity of the skin of the trunk. In this way the arms and legs are exposed less effectively. Because of the higher transmission of the skin for UV-A than for UV-B (20), the extremities are exposed more effectively in the PUVA regimen than in the UV-B regimen. In this way UV-B and PUVA were not given equal chances on the extremities during the comparisons. However, this difference also occurs in practice, when the patients are receiving treatment over the entire skin. Therefore it was decided to deal with the overall impression of the clinical observers where they compared the therapeutic effectiveness on the left and right sides as a whole.

It is noteworthy that only in those 3 cases where the observers were in favour of PUVA, the patient's choice was PUVA too. In all cases where the two therapies were equally effective or UV-B was better, the choice was UV-B. In most cases this was due to the practical advantages of UV-B phototherapy. For the patients it is less time consuming and it gives a smaller heat-load during the exposures; about half as many lamps are needed and still shorter exposure times suffice, especially at the beginning of the treatments. With UV-B therapy the patients do not have to fear a phototoxic reaction to sunlight, nor do they have to wear sunglasses. Moreover, UV-B therapy does not cause as many side effects as PUVA does.

In previous studies the mean remission period ($\pm$SD) after treatment with the narrow-band UV-B

lamps (13) (5.5 ± 3.5 months) was not significantly different from the remission periods after PUVA (8) (5.2 ± 2.8 months). Therefore, the remission period is not a decisive consideration in the choice between these two therapies.

Besides the therapeutic effectiveness, the carcinogenic risks of both PUVA and narrow-band UV-B are important for the choice of therapy. In a risk evaluation study Slaper et al. (21) concluded: "A comparison of the model prognoses for UV-B therapy with the observed risk among PUVA-treated patients in the U.S.A. shows a much higher observed risk for squamous cell carcinomas among the PUVA-treated patients." The UV-B therapy referred to in that study was given with broad-band UV-B. The conclusion can only be fortified by the results of two studies (13, 22) in which the narrow-band UV-B is even less carcinogenic than the broad-band UV-B.

If we take into account the data on effectiveness, side effects, remission period and long-term risks it appears advisable to start treating psoriasis patients with narrow-band UV-B rather than with PUVA. If UV-B therapy is not effective one can try PUVA as an alternative.

In conclusion: narrow-band UV-B phototherapy on a twice-a-week treatment schedule is on average as effective as PUVA photochemotherapy; it is certainly more convenient for the patient, and probably less carcinogenic.

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