UV-B Phototherapy Clears Psoriasis Through Local Effects

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Objective: To determine if UV-B phototherapy clears psoriasis through systemic effects.

Design: Randomized, within-subject comparison of change in psoriasis in 3 plaques in patients attending for whole-body UV-B therapy. Change in patients' psoriasis plaques covered during UV-B treatment was compared with plaques in an untreated control group.

Setting: University hospital phototherapy unit.

Patients: The study population comprised 17 patients with chronic plaque psoriasis treated with UV-B and 24 psoriasis control patients awaiting UV-B phototherapy.

Interventions: Treatment with a standard 3-times weekly narrowband TL-01 UV-B regimen. Three similar plaques were randomly allocated to be covered every treatment, covered for 2 of 3 weekly treatments, and exposed to local UV-B every treatment. Similar plaques were selected in control patients (awaiting but not yet started UV-B therapy). Severity of psoriasis plaques was assessed using a scaling, erythema, and induration (SEI) scoring system.

Main Outcome Measures: Change in SEI score of the selected plaques over the complete treatment course for UV-B–treated patients and change over 3 weeks in SEI score of plaques covered during UV-B treatment compared with that of plaques in controls.

Results: There was a significant ($P<.001$) difference in how much the SEI score changed in the 3 plaques in UV-B–treated patients. It fell by a mean of 7.6 for uncovered plaques compared with 3.2 for plaques covered during each UV-B exposure (95% confidence interval for difference, 3.0 to 5.8). In patients awaiting UV-B, SEI score of plaques fell by a mean of 0.4 over 3 weeks, compared with a mean fall of 1.4 for covered plaques in UV-B-treated patients (95% confidence interval for difference in means, 0.1 to 2.0).

Conclusions: If UV-B therapy has any systemic effect capable of improving psoriasis, this effect is small and unlikely to be of clinical importance. It is insufficient to alter interpretation of findings of within-subject comparative phototherapy studies. UV-B phototherapy works for chronic plaque psoriasis through local effects.

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Does UV-B phototherapy clear psoriasis through direct local effects, systemic effects, or a combination of both? The answer to this has implications for the interpretation of within-individual comparisons of different phototherapy regimens. It should also contribute to our attempts to understand how UV-B works.

Conceivably, UV-B may work to clear psoriasis on sites not directly irradiated. Ultraviolet B has various effects on parameters of immune function detectable in the circulating blood. Whole-body broadband UV-B treatment of humans has effects on the function of blood neutrophils, and narrowband TL-01 UV-B reduces circulating natural killer cell activity. In mice, systemic inhibition of induction of delayed type hypersensitivity appears to be mediated by UV radiation–induced interleukin 10 release. According to findings from laboratory studies, UV-B may have anti-inflammatory effects resulting from the release of neuropeptides from the skin into the circulation. In healthy human volunteers, systemic effects of UV-B on nonimmunological responses to benzoic acid and methyl nicotinate have been reported. Also, increased activity of interleukin 6 and tumor necrosis factor $\alpha$ may be important in systemic symptoms associated with sunburn, and therapeutic broadband UV-B leads to increased interleukin 1 activity. Such demonstrated systemic effects could possibly be relevant in psoriasis clearing.

Other treatments have been reported to have a systemic effect on psoriasis clearing.
PARTICIPANTS AND METHODS

STUDY PROTOCOL

Design and Patients

This study was a prospective, randomized, controlled, interventional study approved by the Tayside Committee on Medical Research Ethics. Consecutive patients with chronic plaque psoriasis referred to the phototherapy unit at Ninewells Hospital and Medical School (a university hospital serving Tayside, Scotland) between April 1998 and June 2000 were invited to participate. Exclusion criteria were age younger than 18 years; a history of skin cancer or solar keratoses; or phototherapy, psoralen-UVA therapy, or systemic therapy for psoriasis within the preceding 3 months. The enrollment criteria for patients treated with phototherapy during the study and the concurrently recruited control group (awaiting but not yet started phototherapy) were identical.

Treatment Regimen

Ultraviolet B phototherapy was administered according to our standard regimen. The starting dose was 70% of each individual’s minimal erythema dose, with 20% increments, reduced to 10% according to erythemal response. Either a Waldmann UV3000 cabinet (Herbert Waldmann GmbH & Co KG, Villingen-Schwenningen, Germany) fitted with 24 Philips 100W TL-01 lamps (Philips, Eindhoven, the Netherlands) or a cabinet constructed at the Ninewells Medical Physics Department with 50 Philips 100W TL-01 lamps was used.

Adjunctive therapy was limited to emollients known not to significantly impede UV transmission and standard topical treatments for scalp, face, and flexures. End points for stopping therapy were, as in our routine practice, clearance (no palpable psoriasis remaining) or “minimal residual activity,” defined as trace disease, below knees or on sacrum only. To give all patients a chance of achieving complete clearance, treatment was started either at clearance or after the fourth treatment at which minimal residual activity was documented, whichever came first. The control patients awaiting phototherapy were permitted the same topical therapy (emollients and scalp and flexure treatments) as those treated with UV-B.

Study Interventions

For the group attending for phototherapy, 3 similar plaques on the trunk or limbs were selected before treatment was started. Only plaques above the knees were selected on lower limbs. These were assessed for scaling, erythema, and induration scores (see “Outcome Measures”) and randomly allocated (as described under “Assignment”) to the following interventions: 1 was covered with Tegaderm dressing (3M Health Care, St Paul, Minn) with backing kept on (which allowed no UV radiation transmission when assessed with Hitachi U-3210 [Tokyo, Japan] double-beam reflectance spectrophotometer) during each treatment, 1 was kept uncovered (ie, exposed normally during treatment), and 1 was covered for 2 of the 3 treatments delivered each week (and treated independently following the same standard regimen as for whole-body exposure). This once-weekly exposed plaque was included because we hypothesized that systemic effects might only significantly influence psoriasis clearing in conjunction with some “priming” UV-B exposure.

For the control group, a single plaque, similar to the selected plaques in the patient group receiving phototherapy, was chosen in each of 24 patients referred for, but not yet receiving, phototherapy. Topical therapies for these patients were limited to the same preparations as were allowed for the phototherapy patient group. Scaling, erythema, and induration score for this plaque was recorded at baseline and 3 weeks later (or as soon after as feasible).

RESULTS

Seventeen patients attending for UV-B phototherapy and 24 control patients awaiting phototherapy participated in the present study (Table). All those attending for UV-B phototherapy completed the study. Of the control patients, 5 did not complete the study: 3 withdrew (1 to start UV-B immediately, 1 used a coal tar solution cream, 1 moved and started UV-B therapy elsewhere), and 2 did not have their selected plaques assessed at their second (pre-UV-B therapy) visit.

Phototherapy patients and controls were similar in age, sex ratio, and skin phototypes (Table). Within these
groups, the psoriasis responded to a similar degree, as indicated by the almost identical treatment numbers and UV-B dose required for treatment.

ANALYSIS

Group Attending for Phototherapy
(Within-Patient Comparisons)

Most plaques improved over the period from the beginning of the UV-B treatment course to the end of the course (Figure 1). There was a significant (P<.001) difference in how much the SEI score changed between the 3 plaques (covered during treatment, covered for 2 of 3 treatments per week, or exposed during treatment). The mean reduction in SEI score was 7.6 for plaques directly exposed to UV-B compared with 3.2 for plaques covered during each UV-B exposure, that is, a greater reduction in mean SEI score of 4.4 (95% confidence interval [CI], 3.0–5.8) in the normally exposed plaques. The difference in clinical appearance of psoriasis covered during each treatment and neighboring exposed psoriasis was clear by the end of most patients’ treatment courses (Figure 2). There was no significant difference between the mean fall in SEI score for covered vs once-weekly exposed plaques (95% CI, −0.8 to 2.0). The markedly greater decline in mean SEI score throughout the treatment courses in the 3-times weekly exposed plaques compared with the covered and once-weekly–exposed plaques is shown in Figure 3.

Control Group

Initial comparison of change in SEI score over 3 weeks for covered plaques in phototherapy patients with change from baseline to second assessment (≥3 weeks [mode, 3½ weeks; median, 4 weeks]) for control patient plaques showed no significant difference. The mean score for covered plaques in phototherapy patients fell by 0.4 (95% CI, −0.4 to 1.3) more than the mean control patient plaque score. When the change in score for control plaques was corrected (to allow a fairer comparison, since control plaques were assessed at intervals up to a maximum of 7 weeks after initial assessment), the difference remained small and of no likely clinical importance, although it was unlikely to have occurred by chance. The mean SEI score
for covered plaques in phototherapy patients fell by 1.0 (95% CI, 0.1-2.0) more than it fell over 3 weeks in control patient plaques (Figure 4).

There were no differences in variables that might influence response of the 3 plaques in patients receiving phototherapy. Prognostic features attributable to the patient as a whole were of course identical, and by random allocation of intervention to the individual plaques, we minimized the possibility that the plaques (allocated to any 1 of the 3 interventions) would be expected to be more or less likely to improve. We attempted to ensure that the plaques in control patients would have similar prognostic variables to the covered plaques in the phototherapy patients.
totherapy patients by selecting a control group of patients referred for phototherapy for chronic plaque psoriasis, that is, a group expected to have similarly severe psoriasis. In practice, this group showed similar responses to treatment when they received phototherapy after the study (Table).

**COMMENT**

The present study has shown that narrowband TL-01 UV-B phototherapy does not have a clinically important systemic effect contributing to its ability to clear psoriasis. It also showed that once-weekly treatment for up to 10 weeks has little effect on psoriasis. If, as we had hypothesized, UV-B therapy cleared psoriasis through a combination of systemic effects and minor local exposure, then we would have expected a much greater reduction of psoriasis severity in the once-weekly-treated plaque. Incidentally, this study makes it clear that once-weekly treatment of psoriasis would be inappropriate; even if once-weekly treatment might eventually clear psoriasis, it would be unacceptably slow.

To our knowledge, there has been no previous study attempting to determine whether systemic effects of UV-B, or any other form of phototherapy, contribute to psoriasis clearance. One earlier study assessed the possible systemic effect of dithranol treatment. It studied did not include a control group, although the magnitude of improvements in plaques not directly treated suggested a systemic effect, possibly related to effects resulting from clearing of psoriasis elsewhere rather than directly due to dithranol application. We included a control group in our study because we expected some improvement in the study plaques, regardless of the presence or absence of systemic UV-B effects. Such improvement, as observed in the covered plaques of the phototherapy patients in our study (Figure 3), was expected as a result of the following:

- The regression to the mean phenomenon. These patients were all seen when their psoriasis was likely to be worse than usual (to enter the study they had to have sufficiently severe psoriasis to require referral for UV-B). We could anticipate, regardless of any medical intervention, a fall in psoriasis severity from baseline as a result of simple random fluctuation in severity with a downward tendency toward the mean population severity.
- The effects of allowed treatment other than UV-B, that is, the emollients and the encouragement to apply these and possibly the psychological support associated with 3-times weekly attendance.

We aimed to recruit a control group with similar psoriasis to those attending for phototherapy. This meant asking patients with chronic plaque psoriasis referred for UV-B phototherapy to participate. We considered it inappropriate to withhold treatment from such patients for 10 weeks (the maximum duration of a normal treatment course). So, we did not recruit the ideal comparison group of patients requiring, but not yet receiving, UV-B therapy and willing to be treated with emollients alone, while attending for review 3-times weekly for 10 weeks. Although it would have been possible to recruit patients with psoriasis not requiring UV-B as such a control group, it would not have been appropriate. Such patients might be expected to have milder psoriasis and more likely to respond well to emollients and encouragement of regular review alone, so use of such a control group might have hidden a systemic effect of UV-B on the plaques of patients attending for phototherapy. Our compromise was to ensure our control group was similar by recruiting those referred for UV-B therapy, but accepting that we could only ask them to do without treatment for 3 weeks (not unreasonable, since we then had such a waiting list to start treatment) and not insisting on them making extra visits 3 times weekly while not being treated.

As not all control patients were assessed at 3 weeks, we corrected their second SEI score to that expected at 3 weeks, making the assumption that control patient plaques showed an equal rate of decline in SEI score. If we did not do this and compared the change over 3 weeks in phototherapy patients, there would be no significant difference, but with correction for the fact that several control patients had longer than 3 weeks to improve, the SEI score fell significantly more in the covered plaques of UV-B treated patients. However, it should be noted that this difference in fall in SEI scores was small, and although unlikely to be a chance finding, was not large enough to be clinically important. It is probable that such a small difference in decline in SEI score can be explained by the fact that the patients receiving phototherapy were encouraged to apply emollients during their 3-times weekly visits, while the controls were not. It remains possible that a systemic UV-B effect contributed to this slightly greater improvement in the covered UV-B–treated patient plaques, but such an effect would have to be minor.

We conclude that UV-B has no clinically important systemic effect on psoriasis clearance and that the possibility of what seems to be at most a minor systemic effect should not influence our interpretation of within-subject study comparisons of UV-B phototherapy regimens for psoriasis. Ultraviolet B phototherapy works for psoriasis through local effects.

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**REFERENCES**


