Efficacy of the 308-nm excimer laser for treatment of psoriasis: Results of a multicenter study

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Objective: Our purpose was to demonstrate the efficacy of the 308-nm excimer laser for treatment of psoriasis.

Methods: This study was a multicenter open trial from 5 dermatology practices (one university-based and 4 private practices). Up to 30 patients per center with stable mild to moderate plaque-type psoriasis constituted the study population. Patients received 308-nm ultraviolet B doses to affected areas. The initial dose was based on multiples of a predetermined minimal erythema dose. Subsequent doses were based on the response to treatment. Treatments were scheduled twice weekly for a total of 10 treatments. The main outcome measure was 75% clearing of the target plaque. Time to clearing was analyzed by Kaplan-Meier methods, accounting for truncated observations.

Results: One hundred twenty-four patients were enrolled in the study, and 80 completed the entire protocol. The most common reason for exiting from the study was noncompliance. Of the patients who met the protocol requirements of 10 treatments or clearing, 72% (66/92) achieved at least 75% clearing in an average of 6.2 treatments. Eighty-four percent of patients (95% confidence interval [CI], 79%-87%) reached improvement of 90% or better after 10 or fewer treatments. Fifty percent of patients (95% CI, 35%-61%) reached improvement of 90% or better after 10 or fewer treatments. Common side effects included erythema, blisters, hyperpigmentation, and erosions, but they were well tolerated.

Conclusions: Monochromatic 308-nm excimer laser treatment appears to be effective and safe for psoriasis. It requires fewer patient visits than conventional phototherapy, and, unlike those treatments, the laser targets only the affected areas of the skin, sparing the surrounding uninvolved skin. (J Am Acad Dermatol 2002;46:900-6.)

O
f the treatments for extensive psoriasis, ultraviolet B (UVB) phototherapy has one of the greatest benefit/risk ratios.1 Broadband UVB phototherapy is a well-established and effective treatment for psoriasis, typically requiring 25 or more treatments for a course of therapy.2,3 A recent refinement to this phototherapy has been narrowband 311-nm UVB phototherapy, which utilizes the most effective wavelengths of the UVB action spectrum (300-313 nm) for psoriasis.4 Narrowband UVB phototherapy has consistently been shown to be safe and effective for psoriasis.5-10 UVB phototherapy is not generally used as a primary treatment for localized psoriasis; this may be due to multiple factors. The inconvenience of numerous office visits may outweigh potential benefits. There may be a relatively lower benefit/risk ratio when extensive areas of normal skin are exposed in the treatment of a very limited area of disease. There also may be a relatively better benefit/cost ratio for topical treatments when only limited areas are treated. Nevertheless, the effectiveness of topical therapy is generally not as great as that of phototherapy.11 Remissions, which may be seen with phototherapy, are generally not associated with...
topical treatments. The remittive effects of phototherapy are thought to be due to UV-induced apoptosis of activated intraepidermal T cells involved in the pathogenesis of psoriasis. Moreover, UV treatment of psoriasis can clear all the histologic manifestations of the condition; some of the histologic abnormalities of psoriasis remain after either topical corticosteroid or systemic therapy with methotrexate. This, too, may explain the remittive properties of phototherapy.

Psoriasis has considerable impact on patients' quality of life, and the troublesome character of currently available treatments is one of the more bothersome aspects of the disease. Development of an effective methodology to treat localized psoriasis with UVB could offer many advantages over current therapies for localized psoriasis. A 308-nm excimer laser using a xenon-chloride (XeCl) lasing medium showed promise in the treatment of 10 patients with localized psoriasis. By not treating uninvolved skin, considerably higher doses of UVB can be administered to the psoriasis plaques at a given treatment; doses as high as 6 times the minimal erythema dose (MED) for normal skin were well tolerated by the psoriasis plaque. Clearing of psoriasis with this laser may occur with as few as 4 treatments without blistering. These studies suggest that use of this laser may provide a relatively convenient treatment that spares uninvolved skin and avoids the unwanted effects of topical treatments.

Previous studies have not provided sufficient efficacy data to fully assess whether the 308-nm laser is a viable treatment for localized psoriasis plaques. In this study, the XTRAC 308-nm excimer laser (Photomedex, Radnor, Pa) recently approved by the Food and Drug Administration, was used to assess the effectiveness of a multiple MED dosing of psoriatic plaques in a multicenter environment.

**PATIENTS AND METHODS**

The study was performed in 5 dermatology offices, one of which was a university-based practice. Commercial and institutional review boards approved this study. Informed consent was obtained before the start of the study. Adults with stable, mild to moderate plaque-type psoriasis vulgaris involving less than 10% body surface area were recruited. Stable plaques were defined as those that had been present and unchanged for a minimum of 2 months. Patients who had received or had completed systemic treatments (eg, methotrexate, cyclosporine, hydroxyurea, retinoids) within the past 8 weeks were excluded. Also excluded were patients who had received any other form of phototherapy within the past 4 weeks or had used topical treatments (other than emollients such as mineral oil) within the past 2 weeks on the sites to be treated with the excimer laser. Patients who had a history of nonresponse to UVB phototherapy, koebnerization, or hand or foot involvement with psoriasis were also excluded. The laser was an XTRAC XeCl excimer (Photomedex, Radnor, Pa) with output consisting of monochromatic 308-nm light with a pulse width of 30 ns and a fiberoptic delivery system connected to a hand piece. Nominal output was 10 mJ per pulse, and the laser could be operated at up to 200 pulses per second. The spot size of the UV light delivered to the patient was 3.2 cm², with a nominal fluence of 3 mJ/cm² per pulse.

Before the first treatment, each patient's MED was determined on unexposed, uninvolved skin. The MED was defined as the minimal fluence of laser light capable of producing well-defined, macular, pink erythema. Delivered fluences were 100, 150, 200, 250, 300, and 350 mJ/cm², corresponding to MED levels of 1 through 6. Evaluation of each patient's MED was scheduled for 24 hours after administration of the dose, although in some cases the interval was longer. Each patient's MED was determined as the energy setting that caused a detectable pinkness.

The initial UV dose administered was based on the MED and the physical characteristics (location, size, thickness) of the plaque. An initial dose of 3 MED was generally used. Plaques on the ankles or intertriginous areas were treated with 2 MED. Tanned plaques were treated with additional 1 MED. If blistering occurred, petrolatum (Vaseline) or hydrophilic petrolatum (Aquaphor healing ointment) was applied; the dose of the subsequent treatment was reduced by 1 multiple (14%-50%); and the blistered plaque was not treated on the next scheduled treatment. The initial dose was maintained until plaques thinned or flattened considerably or pigment appeared. Once plaques thinned or became hyperpigmented (or both), the dose was reduced by 1 MED (14%-53%), maintaining erythema. Over the course of treatment, dose was continually reduced by 1 MED as plaque continued to thin or become hyperpigmented, or both. If the lesion did not respond visually (no flattening, tanning, or reduction or scale), the patient did not indicate a sensory response (sunburn sensation, tenderness), and/or there was no evidence of erythema after the first treatment, dose was increased by 1 MED. The dose was increased by 1 MED on subsequent treatments if no response was indicated. For lesions that did not clear (clearing was defined as >90% improvement)
after 10 treatments, treatments were halted and subject evaluation performed.

If thick scale was present, 12% ammonium lactate (Lac-Hydrin) lotion or equivalent was applied as a descaling agent twice daily after bathing or showering for several days before laser treatment. Immediately before laser irradiation, a small amount of mineral oil was applied to the area to be treated to clarify the scale.

A target plaque in each patient was selected. Photographs were taken of major areas of involvement and of the target plaque. A global whole-body Psoriasis Area and Severity Index (PASI) score and a local (modified) PASI score were recorded for the target plaque. The modified PASI score included scaliness, redness, and induration of the target plaque. Treatments were scheduled twice weekly with a minimum of 48 hours between treatments. The total treatment period was 10 treatments.

Clinical evaluation (global and modified PASI score) was performed at baseline (before first treatment), at the 4th treatment (5th visit), after the 10th treatment (11th visit), and on clearing if clearing occurred. Photographs were taken at baseline, on clearing if clearing occurred, and after 10 treatments.

**Statistical analysis**

Time-to-event analyses were performed on thresholds for clearing equal to 75% and 90% in the target plaque by using the Kaplan-Meier method to account for truncated observations. These two outcomes were selected for analysis based on their use in other psoriasis treatment studies. The starting point for analyses was the first clinical evaluation after the 10th treatment (or last treatment, if earlier). Observations were censored in patients who dropped out of treatment without restarting during the study or who completed the protocol without attaining the percent-clearing threshold.

**RESULTS**

One hundred twenty-four patients were enrolled in the study. Enrolled subjects (57% male, 43% female) had a mean age of 46 years (standard deviation [SD] = 14.8 years). The age at onset of psoriasis ranged from 4 to 77 years, with a mean of 30.8 years (SD = 16.6 years). The Fitzpatrick skin types ranged from I to IV (Table I). The skin type of 76.5% of the subjects was II-III. Among enrollees, 116 were evaluated clinically after one or more treatments and were thus included in analyses. Eighty patients completed the full treatment protocol. Of patients who did not complete the protocol, the most common reason for exiting from the study was noncompliance, in the form of missed appointments and unreturned telephone calls. Other common reasons included incorrect evaluation, conflict with work schedule or not enough time, and unrelated health problems (Table II), but not adverse events.

Of the patients who met the protocol requirements of 10 treatments or clearing, 72% (66/92) achieved at least 75% clearing in an average of 6.2 treatments; 35% (28/80) achieved at least 90% clearing in an average of 7.5 treatments (Figs 1 and 2). Two patients achieved 90% clearing in one treatment. The patient counts for the 75% and 90% clearing milestones differ because of patient discrimination before achieving the 90% milestone within the 10-treatment protocol. Subjects were generally pleased with the improvement in their condition;
only 6.8% dropped out of the study because of dissatisfaction with their progress.

Figs 3 and 4 show the Kaplan-Meier curves for the 75% and 90% clearing outcomes, respectively, in the 116 patients. The median number of treatments for 75% improvement in the target plaque was 8 (Fig 3). The Kaplan-Meier estimate of the probability of less than 75% improvement after 4 treatments was 82% (95% CI = 76%-88%), after 6 treatments was 65% (95% CI = 59%-72%), after 8 treatments was 44% (95% CI = 40%-50%), and after 10 treatments was 16% (95% CI = 13%-21%). For example, 84% of patients reached 75% or better improvement after 10 treatments or less. The same results for 90% clearing in the target plaque were 96% (95% CI = 92%-100%), 88% (95% CI = 83%-95%), 83% (95% CI =
77%-90%), and 50% (95% CI = 39%-65%) after 4, 6, 8, and 10 treatments, respectively (Fig 4).

The most common side effect was erythema, occurring in 63 of 124 patients (50.8%). Other common side effects seen in 10% or more of subjects included blisters (45.2%), hyperpigmentation (37.9%), and areas of shallow erosion (25%, Table III). The size and duration of blisters were not recorded. Side effects were generally well tolerated, and no subject discontinued involvement in the study because of adverse events.

**DISCUSSION**

There has been considerable evolution in UV treatment of psoriasis. Broadband UVB phototherapy is generally safe and effective for psoriasis.22 To further enhance phototherapy, the use of narrowband UVB therapy was developed. This approach was based on the finding that short-wavelength UVB is erythemogenic but not therapeutic.4 The use of a longer wavelength narrowband UVB source to treat psoriasis affords greater efficacy.8,9 Our understanding of the scientific basis for UV treatment is also evolving, with a greater understanding of the effect of this therapy on depletion of activated intraepidermal T cells.13,23 This effect may explain the remittive properties of UV treatment of psoriasis and the ability of phototherapy to completely clear all signs of psoriasis, even at the microscopic level.12,16,17

Development of the XeCl excimer laser for psoriasis is another advance. The high-energy UV wavelength, short-pulse XeCl lasers have been used for ablative purposes in industry and medicine, most notably in ophthalmologic surgery (refractive keratoplasties) and in vascular procedures (angioplasty).24,25 Technically, development of this laser as a nonablative treatment for psoriasis is a considerable achievement. A quartz fiber optical delivery system must be used so as not to attenuate the delivery of UV light. The fiberoptic system of this laser must be flexible to facilitate exposure of lesion skin; however, quartz is brittle, so it must be protected from breakage. Finally, it must be de-
signed so as not to degrade over time despite the very high levels of UV energy passing through it.

A UV laser treatment for localized psoriasis would have considerable advantages over current treatments. UV is generally highly effective for psoriasis. It is a safe treatment. Moreover, by treating only lesional skin, an even greater benefit/risk is expected because there will be less risk to the uninvolved skin. In addition, this allows higher doses to be used initially on the psoriasis plaques, resulting in faster clearing and fewer exposures. Finally, UV treatment is a remittive therapy.

In several of these areas, the effectiveness of the 308-nm XeCl excimer laser has been demonstrated. Although conventional UVB typically requires about 25 or more treatments, improvement was seen with the excimer laser within a 10-treatment protocol, including clearing in one treatment. This convenience factor may increase treatment compliance. As expected, the high intensity at which the laser doses are delivered allows for the possibility of a more rapid response in fewer treatments, resulting in the cumulative dose being delivered in a shorter time frame than conventional phototherapy. The high UV intensity does commonly result in erythema and often in blisters, but these side effects appear to be generally well tolerated. Continued follow-up of the patient cohort group and further study will be needed to assess the remittive properties of this approach.

Our study adds considerably to our knowledge of the efficacy of excimer laser treatment of psoriasis. Previous work demonstrated the principle that, at least focally, individual lesions of psoriasis could be cleared with as few as one excimer laser treatment, albeit with high doses that resulted in blistering. Our study demonstrates that overall clinical success can be achieved with clearing of all lesions. Although truncal lesions were studied previously, we found that clearing was achievable in even relatively resistant areas such as the legs, elbows, and knees. Moreover, clinical success may be achieved using a protocol that is sufficiently gentle to be suitable for use in the clinical setting.

Further refinement may be possible because we expect that with greater clinical experience we will be able to improve the efficacy and minimize the number of treatment exposures and adverse events. The use in combination with topical agents (eg, calcipotriene and tazarotene) or oral agents (acitretin) that may be synergistic with phototherapy still needs to be defined. We expect, based on extrapolation from data on UVB phototherapy, that excimer laser treatment will be very safe over the long term. However, there is the potential for unknown risks given the very different dosage schedule that is used with excimer laser treatment compared with that of standard UVB phototherapy.

In conclusion, the 308-nm excimer laser appears to have several advantages over other available treatment modalities for psoriasis, including fewer treatments, and the added safety of site-specific dosing without exposure to healthy skin. In addition, this study has shown the excimer laser to be well tolerated and effective in treating thick, scaled plaques on the knees and elbows, which are often resistant to treatment. The excimer laser holds promise for becoming part of the therapeutic armamentarium for localized, plaque-type psoriasis vulgaris.

REFERENCES