STUDY

308-nm Excimer Laser for the Treatment of Psoriasis

Induration-Based Dosimetry

Atul Taneja, MD; Manju Trehan, MD; Charles R. Taylor, MD

Objective: To determine the response of stubborn psoriatic plaques to the 308-nm excimer laser.

Design: Controlled study with a before-after design.

Setting: A university-based clinical research center.

Patients: Adult subjects with recalcitrant plaque psoriasis that have not responded to other therapies for at least 2 months.

Interventions: Selected psoriatic plaques were treated with the 308-nm excimer laser. One lesion was left as a control. Each plaque was treated 2 times a week, with an initial dose based solely on the induration component of the modified Psoriasis Area and Severity Index score for that lesion. Subsequent treatments were twice a week with dosage increments up to 50%, based on the change in induration. Four final consolidation doses were given once the induration score was reduced to zero.

Results: Eighteen subjects were treated. There were 4 dropouts because of various scheduling problems. In the remaining 14 subjects, 44 plaques received a mean of 10 treatments (range, 4-14). Treatments were quick and well tolerated. The mean cumulative dose was 8.8 J/cm^2 (range, 2.2-22.8 J/cm^2). Compared with controls, treated plaques showed significant improvement ($P<.001$). The only adverse event was a mild sunburn-like reaction in 2 subjects after 1 treatment.

Conclusions: Selective targeting of laser-generated 308-nm excimer radiation with this convenient subblistering dosage schedule based on induration allows for individualized treatment plans for each plaque. Clearing of stubborn psoriatic lesions occurs rapidly and safely.

Arch Dermatol. 2003;139:759-764

From the Gange Photomedicine Research Center, Department of Dermatology, Harvard Medical School, Massachusetts General Hospital, Boston. The authors have no relevant financial interest in this article.

THERE HAVE BEEN several investigations on the use of the 308-nm excimer laser in the treatment of psoriasis.[1-4] Interest in this laser has been growing, given its ability to selectively target and rapidly debulk lesions that have not responded to conventional treatment; however, optimal laser parameters are yet to be determined. Investigators have used various dosage schedules, including high blistering dosages and subblistering dosages. All of these protocols have been based on minimal erythema doses that are determined on normal unaffected skin. Such dosimetry may not be appropriate for treatment of every lesion, because excimer laser pulses are targeted on affected skin alone and plaques differ widely in clinical characteristics of erythema, induration, and scaling. Because this laser can be precisely directed to individual plaques of psoriasis, for this study, we based our dosages solely on the thickness, or the induration, of each plaque, with thicker lesions getting higher dosages and thinner lesions getting lower ones. This dosimetry schedule would appear to be logical and practical. It eliminates the need for a baseline minimal erythema dose test, which appears to be more useful in cases of total body UV light treatment, not localized plaques.

METHODS

SUBJECTS

This study was approved by the institutional review board of the Massachusetts General Hospital. Informed consent was obtained before the start of the study. Only stubborn lesions, unresponsive to other modes of treatment for at least 2 months, were selected for treatment. For this initial investigation, exclusively nonfacial and nongenital plaques were studied. One lesion per subject was selected as a control. An adequate washout period of 2 weeks for topical therapy, 4 weeks for phototherapy, and 8

©2003 American Medical Association. All rights reserved.
Downloaded From: http://archderm.jamanetwork.com/ on 05/21/2013

Dosage Increments Schedule

Weeks' Dosage	Increment, %	Condition
1-2	50	If induration score remains the same
	25	Some improvement seen, but no actual change in induration score
	0	Induration score decreases by at least 1
3-4	40	If induration score remains the same
	20	Some improvement seen, but no actual change in induration score
	0	Induration score decreases by at least 1
5-6	30	If induration score remains the same
	15	Some improvement seen, but no actual change in induration score
	0	Induration score decreases by at least 1
7-10	20	If induration score remains the same
	10	Some improvement seen, but no actual change in induration score
	0	Induration score decreases by at least 1

weeks for any systemic therapy for psoriasis was required before beginning treatment. Patients who were pregnant, lactating, or UV-B photosensitive (eg, xeroderma pigmentosum) were excluded from the trial. A brief medical history was obtained, especially with regard to the patient's psoriasis and medications.

LASER AND DOSIMETRY

The laser was a 308-nm xenon chloride excimer (PhotoMedex Inc, Carlsbad, Calif). The output consisted of a train of short pulses of 30 nanoseconds' duration, at a pulse rate of up to 200 Hz, delivered through a flexible fiberoptic handpiece. The beam cross section was a 1.8×1.8-cm square, with a nominal operating energy of 3 mJ/cm^2 per pulse. This laser can be used in a pulsed tile mode (discrete pulses) and a paint mode (continuous beam). For this study, the tile mode was used. Because of the gaussian distribution of the beam profile, an overlap of 30% was used for adjacent treated sites to compensate for the slight fall in the output at the edges. The total number of pulses to be delivered was controlled by a foot switch.

Subjects and operators were required to wear goggles to protect their eyes during treatments. A modified Psoriasis Area and Severity Index (PASI) score was obtained for each plaque by adding the scores for the erythema, induration, and desquamation components, with scores of 0 to 3 (0, none; 1, mild; 2, moderate; and 3, severe) for each component. Two independent observers (A.T. and Ashley Racette) before each treatment determined these scores, and when there was a variation in the assessment of scores, the lower score was chosen to ensure that the lesion did not receive too high a dose. Standard 35-mm photographs were taken at baseline, every 2 weeks during the treatment, and at each follow-up visit. Skin biopsy samples were obtained in willing subjects at baseline, after 5 treatments, and after the end of the last treatment. A follow-up with evaluation was performed at 2 weeks and then monthly for 6 months after the last treatment.

To better enhance the penetration of the UV radiation, mineral oil was applied to each lesion before treatment. The dosage schedule for initial doses was based on the induration component of the modified PASI score for each lesion. For an induration score of 1, the initial dose was 0.4 J/cm^2; for a score of 2, 0.6 J/cm^2; and for a score of 3, 0.9 J/cm^2. Subsequent dosages were twice a week for a maximum of 20 treatments, with increments as specified in the **Table**. If clearing occurred, treatments were stopped earlier. When macular erythema was achieved in at least 90% of the treated plaque area (induration score of zero), 4 treatments at the last dosage were given for consolidation, with a maximum of 1.5 J/cm^2 for the thicker skin areas, such as the knees and elbows, and 1.0 J/cm^2 for other locations. The maximum dosages were based on our experience with this laser in other protocols. In the event of blistering, further treatments were withheld until the crusts disappeared. Treatments were then restarted at the previous lower dosage. Patients who missed a treatment were also treated at the previous lower dosage.

STATISTICAL ANALYSIS

Improvement scores were calculated for each plaque and its control by subtracting the end-of-treatment modified PASI scores from the baseline scores. *t* Tests were used to assess differences between control and treated plaques.

RESULTS

Eighteen subjects were enrolled. Four subjects could not complete the treatments because of various scheduling problems. Of the 14 subjects who completed the study, there were 5 women and 9 men, all white, with Fitzpatrick skin types ranging from I to III. Before enrollment, 6 subjects were using topical medications alone, 5 were using phototherapy alone or in combination with topical medications, and 3 were using multiple modalities, including systemic agents, topical medications, and phototherapy. Forty-four plaques were treated, 25 of which were on the knees and elbows, 10 on other parts of the extremities, and 9 on the trunk. Baseline induration scores were distributed as follows: score of 1 (n=7), score of 2 (n=32), and score of 3 (n=5). At baseline, the mean modified PASI scores did not differ between the control and treated plaques (6.4 and 6.3, respectively; $P=.31$).

The treatments were quick. Treatment time varied directly with the total area to be treated and the total dose being administered and was generally less than 1 minute for a 10-cm^2 lesion. A few subjects felt a mild warm sensation at the treated sites during irradiation, but most subjects did not feel anything. The treated plaques flattened gradually with subsequent treatment, as illustrated in **Figures 1**, **2**, **3**, and **4** and in **Figures 5**, **6**, and **7**. Changes were noted in the induration and in the scaling components of the modified PASI scores. The erythema component was the last to improve and, in some cases, persisted even after the last treatment according to this specific protocol. Some lesions (30 of 44 plaques) did not flatten evenly, with focal small regions showing lesser improvement than the rest of the plaque (Figures 3 and 7).

Plaques received a mean of 10 treatments (range, 4-14) and a mean cumulative dose of 8.8 J/cm^2 (range, 2.2-22.8 J/cm^2). The mean modified PASI scores of the treated plaques improved steadily as treatment progressed: from 6.2 (control, 6.4) before treatment; to 2.6 (control, 6.2) after treatment 5; to 1.2 (control, 6.9) after treatment 10; to 1.0 (control, 7.0) after treatment 13. These results are graphically depicted in **Figure 8**. Not surprisingly, mean improvement scores were greater for

©2003 American Medical Association. All rights reserved.
Downloaded From: http://archderm.jamanetwork.com/ on 05/21/2013

Figure 1. Large, thick psoriatic plaque on an elbow before treatment (induration score, 3).

Figure 2. Same plaque after 5 treatments showing clinically apparent reduction in induration and scaling (induration score, 2).

Figure 3. After 12 treatments, there is flattening of the lesion, with only a few tiny areas with persistent scaling (induration score, 1).

Figure 4. At 1-month follow-up, there is mild focal relapse and resolving postinflammatory hyperpigmentation (induration score, 2).

treated than control plaques ($P<.001$). The only adverse event was a mild sunburn-like reaction in the focal areas in 2 subjects after 1 treatment. This resolved spontaneously after skipping a treatment. There were no blistering reactions or instances of Koebner phenomenon. A tanning reaction was observed in 4 subjects, which faded over 2 to 4 weeks after the last treatment, while 8 subjects had postinflammatory hyperpigmentation that

©2003 American Medical Association. All rights reserved.
Downloaded From: http://archderm.jamanetwork.com/ on 05/21/2013

Figure 5. Another thick psoriatic plaque on an elbow (induration score, 3).

Figure 6. Definite reduction in scaling and erythema after 5 treatments (induration score, 2).

Figure 7. Flattening after 12 treatments, with mild focal persistence in scaling and postinflammatory hyperpigmentation (induration score, 0).

resolved gradually over 2 to 6 months. At follow-up, the mean modified PASI scores of all treated lesions gradually regressed from 1.0 at the time of the last treatment; to 2.0 by the end of the third month; to 3.1 at the 6-month follow-up. The relapse was mild in all cases and mostly focal in 20 of 44 cases (Figure 4).

Histopathologic examination revealed differences with treatment. With subsequent treatments, the characteristic psoriasiform hyperplasia with parakeratosis, elongation of rete ridges, loss of granular cell layer, a

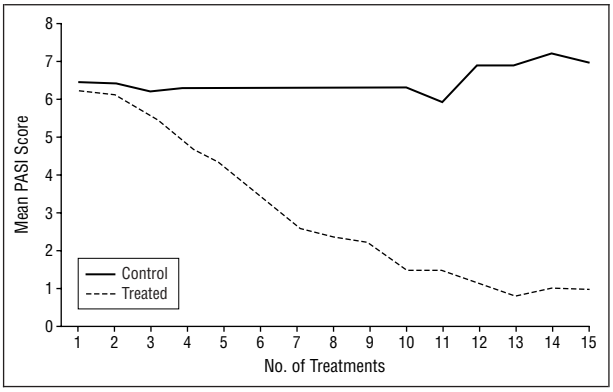

Figure 8. Graphic representation of the reduction in mean Psoriasis Area and Severity Index (PASI) scores of 44 plaques with treatment.

thinned suprapapillary plate, and blood vessels in the superficial dermis was replaced by compact hyperkeratosis, reestablishment of the granular cell layer, mild elongation of the rete ridges, and mild upper dermal lymphocytic infiltrate and then by fairly normal epidermis with only slight pigment incontinence and a hyperpigmented basal cell layer.

COMMENT

The 308-nm excimer laser has been in use for several years and is approved by the Food and Drug Administration for the treatment of psoriasis. Several studies[1-4] have shown that psoriatic lesions improve satisfactorily at high dosages and at medium dosages. We designed our protocol independent of skin type, with dosages based solely on the induration component of each plaque. Such a protocol eliminates the need to do a baseline minimal erythema dose test on each subject. The minimal erythema dose test probably has more relevance in association with total body UV radiation treatments and less so for targeted therapies like the excimer laser. This approach saves time, allowing treatments to occur on the first visit. The initial dose is specifically chosen for each individual plaque, while subsequent doses are based on treatment response and residual plaque induration. In our experience, the other components of the modified PASI score, namely, erythema and scaling, are not so important in determining the appropriate treatment dosage. The variability in scaling within any individual lesion and among different lesions is mitigated by the pretreatment use of mineral oil, which enhances the penetration of light, and thus becomes less important in dose determination. Erythema, the other component of the modified PASI score, remains of uncertain but probably low significance in dose optimization, because other trials[2,3] have demonstrated the ability to give very high dosages without increased complications, despite erythema scores of 4 on the modified PASI scale.

As in other forms of UV phototherapy, we believe that incremental dosages are required when using a subblistering protocol, because the plaque presumably becomes acclimatized to previous dosages and requires a higher dosage for further improvement. One has to balance acclimatization against the fact that as the

©2003 American Medical Association. All rights reserved.
Downloaded From: http://archderm.jamanetwork.com/ on 05/21/2013

plaque becomes thinner the chances of inducing a blistering reaction become higher if the rate of dosage escalation exceeds the protection afforded by tolerance induction. Our gradually tapering dosage schedule allows for adjustment of the dosages, based on the induration response of each individual lesion. When the lesion shows improvement, manifested by decreased induration, the increment for the next dose is automatically lowered in this protocol. Lowering of the increments ensures that the thinning lesions do not get too high a dose, which might result in unwanted burning, blistering, or Koebnerization reactions. To prevent these reactions, we used stepwise 10% increment reductions from 50% through 20% as treatment progressed. Compared with traditional UV protocols that often show continued dosage escalation, sometimes fixed in magnitude until treatment 30, this targeted therapy uses quicker reduction in the increments based on a percentage of the last dose, a method that seems logical because our targeted starting dosages are higher. Given the painless, quick nature of the treatment, our subblistering protocol would seem to lend itself well to patients with more than just a few lesions or with moderate psoriasis and to those who are unable or unwilling to tolerate more aggressive blistering protocols.

The results in our study are comparable to those of other similar clinical trials,[1-4] with lesions showing satisfactory flattening after about 10 treatments. Our trial provides a practical option for using this laser in routine clinical practice. Even thick lesions that are unresponsive to conventional UV-B or narrowband UV-B (NBUV-B) treatment quickly flatten out with proper use of this laser. Admittedly, some lesions did not flatten out evenly, with a few small foci (2%-15% of the original area) that persisted even as the major portion of the plaque dramatically improved. Although one reason for this uneven flattening could be the uneven nature of psoriatic plaques themselves, another plausible explanation is the fall in power at the edges of the beam, which was not completely compensated for even by overlapping, adjacent treatment pulses. A similar explanation might account for the relapses that occurred focally. Notwithstanding that issue, focal relapses occur with all types of psoriasis therapies and may be the way in which a complete relapse starts out. For example, focal relapses may be seen in a plaque of psoriasis that has just cleared on any type of UV therapy, even though the therapy has never stopped. Such an occurrence reflects a deficiency seen with most of our existing therapies for psoriasis. None of the subjects had blistering reactions, but 2 subjects complained of a sunburn-like reaction in the focal areas during 1 treatment. It would seem that the overlapping method we used to compensate for the fall in beam profile at the edges is not exact and can result in focal areas receiving higher doses and some areas getting lower doses.

The tanning response seen in a few subjects faded over a few weeks. However, postinflammatory hyperpigmentation persisted for several months in some of our subjects. This was not bothersome, and all subjects were happy to have their hitherto stubborn psoriatic plaques flattened. For patients with darker skin color, this hyperpigmentation presumably may be more obvious and perhaps of some concern. There may be a role for using adjuvant topical corticosteroids or topical depigmenting agents in these cases.

Comparison of the 308-nm excimer laser with NBUV-B phototherapy is justified, because NBUV-B is being increasingly used in the treatment of psoriasis in many centers around the world. Moreover, the wavelength of NBUV-B at 311 nm is very close to that of the excimer laser at 308 nm. With NBUV-B, in one study,[5] patients showed 78.5% overall improvement in 20 sessions with a mean ± SD cumulative dose of 15.1 ± 3.8 J/cm^2 (range, 8.7-21.7 J/cm^2). In our study, the excimer laser was able to flatten lesions in a mean of 10 treatments and at a mean cumulative dose of 8.75 J/cm^2. Most important, lesions treated with the excimer laser in this study were thick and represented conventional treatment failures, in some cases failing to respond to phototherapy itself. Another advantage of the laser is its focused power, allowing for rapid clearance of lesions, leaving unaffected normal adjacent skin unexposed. This sparing of normal, unaffected skin to unnecessary radiation would seem to be an advantage when considering the short-term and long-term risks of adverse events associated with UV radiation. Long-term follow-up studies are, of course, needed.

The mechanisms for improvement remain open to debate. The proposed mechanisms for improvement of psoriasis with UV-B radiation are complex. One target of UV-B is nuclear DNA, and exposure leads to photoproduct formation (like pyrimidine dimers), which leads to suppression of accelerated DNA synthesis in the hyperplastic psoriatic epidermis and to immunosuppression.[6,7] Moreover, UV-B exposure may alter secretions of soluble mediators like prostaglandin E_2, interleukin 1, interleukin 6, and tumor necrosis factor α, which may alter the cutaneous immune response by direct effects on T lymphocytes or indirectly via the Langerhans cells.[8,9] One other mechanism may be the induction of apoptosis in the psoriatic epidermis.[10] As indicated in a review by el-Ghorr and Norval,[11] TL-01 lamps (Philips Co, Eindhoven, the Netherlands) used in phototherapy may have more suppressive effects than broadband UV-B on systemic immunoresponses, as judged by natural killer cell activity, lymphoproliferation, and cytokine responses. However, the TL-01 lamp may be less effective at reducing epidermal antigen presentation and suppressing contact hypersensitivity. The mechanisms underlying the excimer efficacy may have some features in common with those of broadband and NBUV-B. Definitive investigations are yet to be done.

In summary, this 308-nm excimer laser has a good debulking action in quickly clearing thick recalcitrant psoriatic plaques. Relapses occur as with any other mode of treatment, but we have not observed an unusually high rate of rapid rebound during up to 6 months' follow-up. This laser can serve as an adjunct to other conventional modes of treatment, especially for lesions that are thick and recalcitrant, and as a first choice in patients who have a limited number of lesions. Combination therapy with the excimer laser plus topical therapy seems a logical future research avenue.

©2003 American Medical Association. All rights reserved.
Downloaded From: http://archderm.jamanetwork.com/ on 05/21/2013

Accepted for publication November 5, 2002.

This study was sponsored by PhotoMedex Inc, which provided the laser and subject reimbursement.

We thank Ashley Racette, BS, for her fine technical support; Susan Regan, PhD, for the analysis of the data; and Thomas Flotte, MD, for reviewing the histopathologic findings.

Corresponding author: Charles R. Taylor, MD, Gange Photomedicine Research Center, Department of Dermatology, Harvard Medical School, Massachusetts General Hospital, Bartlett 622, 55 Fruit St, Boston, MA 02114.

REFERENCES

1. Bonis B, Kemeny L, Dobozy A, Bor Z, Szabo G, Ignacz F. 308 nm UVB excimer laser for psoriasis [letter]. *Lancet*. 1997;350:1522.
2. Asawanonda P, Anderson RR, Chang Y, Taylor CR. 308-nm excimer laser for the treatment of psoriasis: a dose-response study. *Arch Dermatol*. 2000;136:619-624.
3. Trehan M, Taylor CR. High-dose 308-nm excimer laser for the treatment of psoriasis. *J Am Acad Dermatol*. 2002;46(pt 1):732-737.
4. Feldman SR, Mellen BG, Housman TS, et al. Efficacy of the 308-nm excimer laser for treatment of psoriasis: results of a multicenter study. *J Am Acad Dermatol*. 2002;46:900-906.
5. Picot E, Meunier L, Picot-Debeze MC, Peyron JL, Meynadier J. Treatment of psoriasis with a 311-nm UVB lamp. *Br J Dermatol*. 1992;127:509-512.
6. Kripke ML, Cox PA, Alas LG, Yarosh DB. Pyrimidine dimers in DNA initiate systemic immunosuppression in UV-irradiated mice. *Proc Natl Acad Sci U S A*. 1992;89:7516-7520.
7. Epstein WL, Fukuyama K, Epstein JH. Early effects of ultraviolet light on DNA synthesis in human skin in vivo. *Arch Dermatol*. 1969;100:84-89.
8. Hruza LL, Pentland AP. Mechanisms of UV-induced inflammation. *J Invest Dermatol*. 1993;100:35S-41S.
9. Yarosh DB, Cruz PD, Dougherty I, et al. FRAP DNA–dependent protein kinase mediates a late signal transduced from ultraviolet-induced DNA damage. *J Invest Dermatol*. 2000;114:1005-1010.
10. Ozawa M, Ferenczi K, Kikuchi T, et al. 312-nanometer ultraviolet B light (narrowband UVB) induces apoptosis of T cells within psoriatic lesions. *J Exp Med*. 1999;189:711-718.
11. el-Ghorr AA, Norval M. Biological effects of narrow-band (311 nm TL01) UVB irradiation: a review. *J Photochem Photobiol B*. 1997;38:99-106.

Archives Web Quiz Winner

Congratulations to the winner of our March quiz, Thaer Douri, MD, Ministry of Health, Hama, Syria. The correct answer to our March challenge was *neutrophilic eccrine hidradenitis*. For a complete discussion of this case, see the Off-Center Fold section in the April ARCHIVES (Crawford GH, Chu AY, Halpern M, James WD. Erythematous facial plaques in a patient with leukemia. *Arch Dermatol*. 2003;139:531-536).

Be sure to visit the *Archives of Dermatology* World Wide Web site (http://www.archdermatol.com) to try your hand at the Interactive Quiz. We invite visitors to make a diagnosis based on selected information from a case report or other feature scheduled to be published in the following month's print edition of the ARCHIVES. The first visitor to e-mail our Web editors with the correct answer will be recognized in the print journal and on our Web site and will also receive a free copy of the *The Art of JAMA II*.

©2003 American Medical Association. All rights reserved.
Downloaded From: http://archderm.jamanetwork.com/ on 05/21/2013