

Comparison of the 308-nm excimer laser and a 308-nm excimer lamp with 311-nm narrowband ultraviolet B in the treatment of psoriasis

K. Köllner, M.B. Wimmershoff, C. Hintz, M. Landthaler and U. Hohenleutner

Department of Dermatology, University of Regensburg, Franz-Josef-Strauss-Allee 11, 93043 Regensburg, Germany

Summary

Correspondence

Katja Köllner MD.

E-mail: katja.koellner@klinik.uni-regensburg.de

Accepted for publication

22 July 2004

Key words:

excimer laser, psoriasis, ultraviolet B

Background Psoriasis is a chronic, genetically determined inflammatory disease, characterized by an immunomediated pathogenesis, which affects approximately 1–3% of the population. Various modalities have been used for psoriasis treatment, including ultraviolet (UV) radiation. Narrowband UVB (311 nm) phototherapy is a well-established, widely used and highly efficient treatment for psoriasis, but a big disadvantage is that large areas of unaffected skin are irradiated along with the psoriatic lesions.

Objectives This investigation evaluates a 308-nm excimer laser and a 308-nm excimer lamp in comparison with 311-nm narrowband UVB in the treatment of patch psoriasis by using two different dose-increase schemes.

Materials and methods Fifteen patients with plaque psoriasis were enrolled in the study (first regime). Three different psoriatic lesions were treated with the 308-nm excimer laser, the 308-nm excimer lamp or 311-nm narrowband UVB three times per week. UVB doses were increased slowly and stepwise (1, 1, 2, 2, 3, 3, ...multiple MEDs). Sixteen patients were enrolled in the second regime. Two plaques were treated with the 308-nm excimer laser or with the 308-nm lamp with an accelerated scheme (2, 2, 4, 4, 6, 6, ...multiple MEDs) three times per week. We increased the UVB doses every second treatment (first and second regime) during the whole treatment. If blistering occurred, the blistered plaque was not treated on the next scheduled treatment. At every third visit and 1, 2 and 4 months after the last treatment a Psoriasis Severity Index (PSI) score was assigned in both regimes.

Results Using Friedman analysis, the PSI scores did not show a statistically significant difference ($P > 0.05$) comparing 308-nm laser therapy, 308-nm lamp therapy and 311-nm narrowband therapy after 10 weeks in the first regime. The mean number of treatments to achieve clearance was 24. With the accelerated scheme, clearance could be achieved with fewer treatments and with half the cumulative dose of the first regime. Nevertheless, the side-effects such as blistering and crusting were also increased.

Conclusions Both 308-nm light sources can clear patch psoriasis in a similar manner to standard phototherapy, with the advantage of the ability to treat exclusively the affected skin and with a reduced cumulative dose, thus perhaps reducing the long-term risk of carcinogenicity.

Psoriasis is a chronic, genetically determined inflammatory disease, characterized by an immunomediated pathogenesis, which affects approximately 1–3% of the population. Cytokines within an established psoriasis plaque are predominantly of the T-helper 1 subtype with a preponderance of interleukin

(IL)-2, IL-12 and interferon- γ and increased levels of tumour necrosis factor- α .¹

Various modalities have been used for psoriasis treatment including ultraviolet (UV) radiation. Narrowband UVB (311 nm) phototherapy is a well-established, widely used

and highly efficient treatment for psoriasis,² which generally requires 25–30 treatments to achieve clearing.³ One of the biggest disadvantages of narrowband UVB (311 nm) phototherapy is that large areas of unaffected skin are irradiated along with the psoriatic lesions. Therefore, patients with circumscribed patch psoriasis are often excluded from light therapy to avoid unnecessary exposure of unaffected skin. On the other hand, the reduced irradiation tolerance of healthy compared with psoriatic skin often does not allow dosage increases as necessary for an optimal resolution.

The 308-nm excimer laser and lamp allow selective irradiation of the affected skin, thus sparing the surrounding normal skin. Narrowband UVB (311 nm) is not very different from the 308-nm radiation generated by the excimer laser and preliminary work has established the efficacy of this new laser in the treatment of psoriasis.^{4–12} Similar good results in the treatment of psoriasis are reported by Campolmi *et al.*¹³ using the 308-nm excimer lamp.

In many of these studies, the cumulative UV dosage and the number of irradiations necessary for resolution were lower than with classical UVB (311 nm) therapy. The single irradiation energies, nevertheless, were quite high leading to erythema, blistering and crusting.^{4–7,10,11,13} The first aim of our study was to evaluate whether 308-nm, either high-frequency pulsed as with the laser or CW with the lamp, has a different biological efficiency compared with the 311-nm fluorescent-lamp light. Therefore, in the first regime, we used slow increases as in classical UVB therapy and compared the three radiation sources with identical treatment schemes. In the second regime, we wanted to evaluate whether 308-nm circumscribed treatment can lead to faster and/or longer-lasting results and whether there might be differences between laser and lamp.

The present investigation (first regime) evaluates the biological effect of the 308-nm excimer laser and the 308-nm excimer lamp in comparison with 311-nm narrowband UVB in the clearing of patch psoriasis by using a slow acceleration scheme. Due to our good experiences and the low rate of side-effects in the first regime, we compared the 308-nm laser with the 308-nm lamp by using a faster and more intensive scheme, in a second study.

Materials and methods

First regime

Fifteen volunteers were included into the study after giving informed consent, the study design being approved by the ethics committee of the University of Regensburg. Those enrolled needed to be 18 years or older, with stable plaque-type psoriasis. All systemic and topical treatments had to have been stopped before the start of the study. Subjects taking medications known to cause photosensitivity and those with a history of photosensitivity disorders were excluded. No additional treatment options were allowed.

The following light sources were used: a xenon-chloride gas, 308-nm excimer-laser (Wavelight Laser Technology AG, Erlangen, Germany, Stella[®], 308 nm, 20 mm, 40 mW cm⁻², 60 ns, 100 Hz); a 308-nm excimer lamp (Wavelight Laser Technology AG, 308 nm, 40–100 mW cm⁻²) and a conventional 311-nm narrowband UVB partial radiation device (Waldmann, Villingen-Schwenningen, Germany, 311 nm, 3.73 mW cm⁻²).

The 308-nm UVB minimal erythema dose (MED) was determined for laser and lamps on unexposed, uninvolved skin of the back before initiation of treatment. The MED was determined with an increasing series of six laser/lamp-generated fluences, namely, 100, 200, 300, 400, 500 and 600 mJ cm⁻² for Fitzpatrick skin type 1–2 and 150, 200, 300, 500, 700, and 900 mJ cm⁻² for Fitzpatrick skin type 3–4. Subjects were instructed to avoid sun exposure in the tested areas until a reading of the MED was performed 24 h later.

Three treatment areas in similar-appearing chronic psoriasis plaques were selected in each volunteer. The laser's spot size was fixed at 20 mm; for the other light sources the lesion was covered with an opaque foil with a 20-mm hole cut out. Only these three spots were treated in this study. Treatment was performed three times per week. The total treatment period was 10 weeks, or until clearing occurred. Beginning with the MED, we increased the UVB doses every second treatment (1, 1, 2, 2, 3, 3, ...multiple MEDs) during the whole treatment period. If blistering occurred, the blistered plaque was not treated on the next scheduled treatment.

Before treatment and at every third visit a Psoriasis Severity Index (PSI) was calculated, which was derived from the standard Psoriasis Area and Severity Index (PASI) score by omitting the area, thus assigning a score of 0–4 (0, none; 1, mild; 2, significant; 3, moderate; 4, severe) for erythema, induration and desquamation. Clinical photographs were taken at each visit. Likewise, follow-up investigations were performed 1, 2 and 4 months after the end of the treatment. Treated areas were also evaluated for side-effects (pigmentation, erythema, blistering, crusting, scarring) at each visit.

The Friedman test was used to test significant improvement comparing the three treatment methods.

Second regime

Sixteen further volunteers with chronic plaque psoriasis were enrolled in the study. Two large, chronic, similar-appearing psoriasis plaques were selected in each patient. The whole psoriatic plaque was treated in each volunteer; one plaque was treated with the 308-nm excimer laser using partially overlapping spots, the other one with the 308-nm excimer lamp, three times per week for 8 weeks, or until clearing occurred.

For the second study, a slightly improved 308-nm excimer laser (Wavelight Laser Technologie AG, TALOS[®], 308 nm, 10, 20 and 25-mm spot size; 4.6 mJ pulse⁻¹, 60 ns, 200 Hz, 200 mW cm⁻¹, independent of the spot size) was used. It was compared with the 308-nm excimer lamp (Wavelight Laser Technologie AG, 308 nm, 40–100 mW cm⁻²) by using

an accelerated scheme, increasing the UVB doses every second treatment (2, 2, 4, 4, 6, 6, ...multiple MEDs). The three available spot sizes of the laser handpiece (10, 20 and 25-mm spot diameter) allowed treatment of the plaques equally by choosing adequate spots with slight overlap. The surrounding unaffected skin was protected with an individually handmade stencil out of cardboard. For the lamp, the skin surrounding the plaques was covered likewise with clothes and/or individually prepared stencils out of cardboard.

Follow-up investigations and evaluation of the results were identical to scheme 1.

Results

First regime

Fifteen subjects with chronic plaque psoriasis were enrolled into the study (nine male and six female) with a mean age of 46 years (range 26–67). The Fitzpatrick skin types ranged from 1 to 3. In nine volunteers, the psoriatic plaques were localized on the upper extremities, in five volunteers on the lower extremities and in one patient on the trunk.

The mean MED was found to be 347 mJ cm^{-2} (range 200–1000 mJ cm^{-2}) for the excimer laser, 253 mJ cm^{-2} (range 100–600 mJ cm^{-2}) for the 308-nm lamp and 407 mJ cm^{-2} (200–900 mJ cm^{-2}) for the 311-nm phototherapy. The cumulative dose of irradiation was $18.3\text{--}110.5 \text{ J cm}^{-2}$ (mean 52.9 J cm^{-2}) for the excimer laser, $23.7\text{--}114.5 \text{ J cm}^{-2}$ (mean 47.3 J cm^{-2}) for the 308-nm lamp and $23.8\text{--}131.0 \text{ J cm}^{-2}$ (mean 64.9 J cm^{-2}) for the 311-nm narrowband phototherapy, respectively. The mean number of treatments to achieve clearance (equal to 90% reduction of PSI score) was 24.

At baseline, the mean modified PSI score for all the treated plaques was 8.6 (range 6–12). Figure 1 shows the PSI score curves for the entire study period. The mean PSI score could be reduced from 8.6 pretreatment to 1.8 after 10 weeks of laser treatment, 2.13 after 10 weeks of 308-nm lamp treatment and 1.1 after 10 weeks of narrowband phototherapy (Fig. 1). Using Friedman analysis, PSI scores after 10 weeks did not show statistically significant differences ($P > 0.05$)

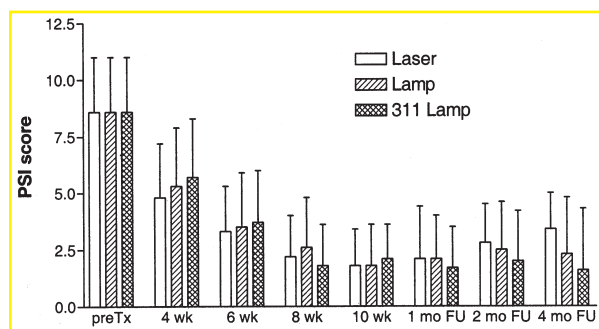


Fig 1. Mean Psoriasis Severity Index (PSI) score after 308-nm excimer laser treatment, 308-nm lamp and 311-nm phototherapy in the first regime.

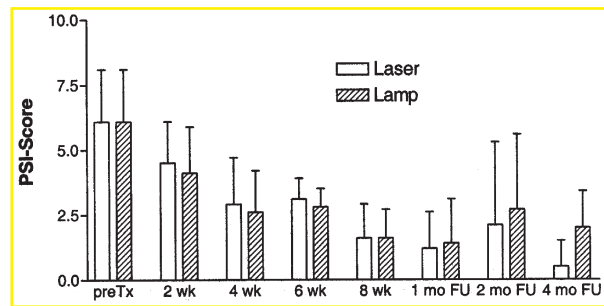


Fig 2. Mean Psoriasis Severity Index (PSI) score after 308-nm excimer laser and 308-nm lamp treatment. Timeline, no. of patients: Pretreatment (preTx), 16; 2 weeks (wk), 16; 4 wk, 15; 6 wk, eight; 8 wk, seven; 1-month follow-up (mo FU), 16; 2 mo FU, seven; 4 mo FU, four.

comparing 308-nm laser therapy, 308-nm lamp therapy and 311-nm narrowband therapy.

After 10 weeks, complete remission was seen in four patients after laser therapy, in three patients after treatment with the 308-nm lamp and in seven patients after 311-nm phototherapy. After 4 months' follow-up, the mean PSI score increased again to 3.4 after excimer laser treatment, 2.3 after 308-nm lamp therapy in comparison with 1.6 after 311-nm phototherapy. No statistically significant difference could be seen ($P > 0.05$). Altogether three patients have still been in remission after 16 weeks.

Side-effects (pigmentation, crusting, blistering, erythema) were seen more often after laser treatment (40.0%) than after 308-nm lamp therapy (26.7%) or 311-nm phototherapy (26.7%). The most common side-effect was hyperpigmentation. No scarring occurred. Treatments were well tolerated by all the participants. No pain sensation was felt during the actual treatment at any time.

Second regime

Sixteen patients with plaque psoriasis were enrolled in the study (nine male, seven female). Mean age was 48.5 (range 33–71) years. The Fitzpatrick skin types ranged from 1 to 3, with 69% of the subjects being type 2. All patients completed the full treatment protocol.

MED ranged from 200 to 400 mJ cm^{-2} (mean 281.3 mJ cm^{-2}) for the laser and from 200 to 300 mJ cm^{-2} for the lamp (mean 231.3 mJ cm^{-2}).

The cumulative dose of irradiation was $3.2\text{--}70.8 \text{ J cm}^{-2}$ (mean 29.17 J cm^{-2}) for the excimer laser and $3.2\text{--}124.2 \text{ J cm}^{-2}$ (mean 37.0 J cm^{-2}) for the 308-nm lamp. At baseline, the mean modified PSI score for all the laser- and lamp-treated plaques was mean 6.1 (range 4–11). After 8 weeks of laser and lamp treatment, PSI scores decreased to mean 1.6 (range 0–3) for both therapy modalities. The mean number of treatments to achieve clearance for the 16 subjects was 13.5. After the 4-month follow-up the PSI score decreased, because only four patients participated regularly since the last follow-up and have been still in remission. Figure 2 displays the PSI

score time line for the entire study period (second regime). Figures 3–5 show an example of a psoriatic lesion on the foot of one patient at baseline, after 19 laser treatments and at the third follow-up.



Fig 3. Psoriatic lesion at baseline (second regime).



Fig 4. Psoriatic lesion after 19 treatments (cumulative dose 4 minimal erythema doses) (second regime).



Fig 5. Psoriatic lesion at the third follow-up (second regime).

Side-effects could be seen in every patient (erythema, blistering, crusting or hyperpigmentation). The most common side-effect was erythema in both therapy modalities, occurring in 13 (81%) patients treated with the laser and in 12 (75%) patients treated with the lamp. Other common side-effects including blistering were seen in 10 patients (63%) treated with the laser and in seven patients (44%) treated with the 308-nm lamp. Hyperpigmentation occurred in 12 laser patients (75%) and 11 lamp patients (69%). Side-effects were generally well-tolerated, and no subject discontinued involvement in the study because of side-effects. The hyperpigmentation gradually faded during the follow-up period. Altogether, side-effects were seen more often in the laser treatment than in the 308-nm lamp treatment similar to the first regime.

Discussion

The most effective spectrum of UVB phototherapy in psoriasis was shown to be between 300 and 313 nm.² This inspired the development of narrowband phototherapy producing 311-nm radiation. Regularly, 311-nm narrowband UVB treatment requires 25–30 treatments to achieve clearance, and large areas of unaffected skin are unavoidably exposed to UV radiation. Long-term patient follow-up studies regarding skin cancer development in patients treated with narrowband UVB phototherapy are still lacking.

Theoretically, the 308-nm laser/lamp offers some advances over current therapy modalities in the treatment of localized psoriatic plaques. Lesional skin can be treated exclusively with less risk for the uninvolved surrounding skin, and preliminary studies have indicated that higher dose-increase schemes are possible, leading to faster healing and reduced cumulative dosis.^{4–10}

Bonis *et al.*⁴ were one of the first who reported that the 308-nm excimer laser was useful in the treatment of psoriasis. The protocol used in this study involved stepwise dose increments similar to conventional phototherapy, nevertheless showing a clear reduction of treatment time and cumulative dosage by using the laser.

In our study (first regime) we used stepwise dose increments as in conventional phototherapy to compare the three radiation sources. Neither the PSI scores nor the cumulative doses showed statistically significant differences ($P > 0.05$) comparing 308-nm laser therapy, 308-nm lamp therapy and 311-nm narrowband therapy, which is contrary to results of Bonis *et al.*

In a recent multicentre study an average of 10 treatments was needed to obtain clearance. Eighty patients completed the entire protocol; 72% achieved at least 75% clearance in an average of 6.2 treatments; 84% of patients reached 75% improvement after 10 treatments; 50% of patients reached 90% improvement after 10 treatments. Side-effects such as erythema, blisters, hyperpigmentation and erosions, nevertheless, were common, if well-tolerated.¹⁰

Other studies have established that psoriatic lesions can tolerate much more UV light than adjacent healthy skin and clear

even faster if higher doses of UV light are selectively delivered to the psoriatic lesion. Asawanonda *et al.*⁶ completed a dose-response study using the excimer laser for the treatment of chronic plaque psoriasis. Doses up to 16 MED multiples were applied to one plaque. Areas receiving high fluences improved more than areas receiving medium or low fluences, and a better response was also seen with increased treatment frequency. Side-effects such as blistering, erosion and crusting, nevertheless, cannot be avoided with such high doses, but show a clear reduction of treatment time and cumulative dosage. Single high-dose 308-nm excimer-laser treatment for limited plaque-type psoriasis was also evaluated by Trehan *et al.*¹¹ Eleven of 16 subjects achieved substantial improvement with reduction of the plaque to a red macule, but blistering, crusting and erosions have to be accepted.

Campolmi *et al.*¹³ was the first to report on 308-nm lamp treatment in palmoplantar psoriasis. Eleven patients were treated for 10 weeks with a 308-nm lamp. After 6 weeks of treatment all patients showed an improvement varying from 75% to 100%. Studies comparing 311-nm narrowband therapy with 308-nm lamp treatment in psoriasis are lacking until now.

The most common side-effects with the 308-nm excimer laser using lower doses are erythema and hyperpigmentation localized to the treated areas. With high and ultra-high (8–16 MED) doses, blistering, erosions and crusting are unavoidable; on the other hand, good results are possible in a short time lasting for months.⁶

In our opinion, bullous sunburns being one of the established risk factors for melanoma, one should discuss whether bullous and erosive reactions can be accepted in phototherapy. Although only psoriatic skin is treated, a risk of long-term carcinogenicity after ultra-high dose exposures cannot, in our opinion, be excluded. Therefore, in our study we decided to avoid these reactions, if possible. This might be one reason that more treatments and a higher cumulative dose were required to achieve clearance of the psoriatic plaques in our study comparing the studies of Bonis *et al.*⁴ and Trehan *et al.*⁷

Better results might be achieved by moistening the psoriatic plaque with mineral oil to enhance the penetration of the radiation.⁷ In all of the studies mentioned above, phototherapy was used as single therapy and no further treatments were allowed. The combination of UVB phototherapy with other conventional therapies such as dithranol or calcipotriol yields probably even better therapeutic effect.^{14,15}

According to our results, in the classical low-dose-increase-scheme there are no advantages of 308-nm radiation except the sparing of uninvolved skin. Using higher doses, the frequency of side-effects clearly increases.

In conclusion, the 308-nm excimer lasers and lamps are clearly effective in the treatment of patch psoriasis. Whether

the sparing of uninvolved skin, the lower cumulative dosage and the shorter treatment, at the cost of increased side-effects such as burn or blistering, are really a therapeutic advancement, in our opinion still remains to be determined by larger and longer-term studies, especially if one takes into account the high cost, especially of the laser treatment. Nevertheless, the possibility of circumscribed UV therapy seems interesting for a variety of other chronic inflammatory localized dermatoses such as granuloma annulare, lichen ruber planus,¹⁶ lichen simplex chronicus, alopecia areata and vitiligo.

References

- 1 Kirby B, Griffiths CE. Psoriasis: the future. *Br J Dermatol* 2001; **144** (Suppl. 58):37–43.
- 2 Parrish JA, Jaenicke KF. Action spectrum for phototherapy of psoriasis. *J Invest Dermatol* 1981; **76**:359–62.
- 3 Gupta G, Long J, Tillman DM. The efficacy of narrowband ultraviolet B phototherapy in psoriasis using objective and subjective outcome measures. *Br J Dermatol* 1999; **140**:887–90.
- 4 Bonis B, Kemeny L, Dobozy A *et al.* 308 nm UVB excimer laser for psoriasis. *Lancet* 1997; **350**:1522.
- 5 Kemeny L, Bonis B, Dobozy A *et al.* 308-nm excimer laser therapy for psoriasis. *Arch Dermatol* 2001; **137**:95–6.
- 6 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**:619–24.
- 7 Trehan M, Taylor CR. Medium-dose 308-nm excimer laser for the treatment of psoriasis. *J Am Acad Dermatol* 2002; **47**:701–8.
- 8 Rodewald EJ, Housman TS, Mellen BG, Feldman SR. The efficacy of 308 nm laser treatment of psoriasis compared to historical controls. *Dermatol Online J* 2001 Dec.; **7**:4.
- 9 Rodewald EJ, Housman TS, Mellen BG, Feldman SR. Follow-up survey of 308-nm laser treatment of psoriasis. *Lasers Surg Med* 2002; **31**:202–6.
- 10 Feldman SR, Mellen BG, Housman TS *et al.* Efficacy of the 308 nm excimer laser for the treatment of psoriasis: results of a multicenter study. *J Am Acad Dermatol* 2002; **46**:900–6.
- 11 Trehan M, Taylor CR. High-dose 308 nm excimer laser for the treatment of psoriasis. *J Am Acad Dermatol* 2002; **46**:732–7.
- 12 Spann CT, Barbagallo J, Weinberg JM. A review of the excimer laser in the treatment of psoriasis. *Cutis* 2001; **68**:351–2.
- 13 Campolmi P, Mavilia L, Lotti R *et al.* 308 nm monochromatic excimer light for the treatment of palmoplantar psoriasis. *Int J Immunopathol Pharmacol* 2002; **11**:11–13.
- 14 Storbeck K, Holzle E, Schurer N *et al.* Narrow-band UVB (311 nm) versus conventional broad-band UVB with and without dithranol in phototherapy for psoriasis. *J Am Acad Dermatol* 1993; **28** (2 Part 1):227–31.
- 15 Kragballe K. Combination of topical calcipotriol (MC 903) and UVB radiation for psoriasis vulgaris. *Dermatologica* 1990; **181**:211–14.
- 16 Köllner K, Wimmershoff M, Landthaler M, Hohenleutner U. Treatment of oral lichen planus with the 308-nm UVB excimer laser—early preliminary results in eight patients. *Lasers Surg Med* 2003; **33**:158–60.