Photodermatol Photoimmunol Photomed 2007; 23: 10–14
Blackwell Munksgaard

Photodermatology
Photoimmunology
& Photomedicine

Local narrowband UVB phototherapy vs. local PUVA in the treatment of chronic hand eczema

Engin Sezer[1], Ilker Etikan[2]

[1]*Departments of Dermatology, and* [2]*Biostatistics, Gaziosmanpasa University School of Medicine, Tokat, Turkey*

Background: **Hand eczema is a chronic skin disorder characterized by a poor response to conventional therapies. Although local PUVA has been proven to be effective in the treatment of chronic hand eczema, little is known about the efficacy and safety of local narrowband UVB (TL-01) for this condition. The aim of our study was to compare the efficacy and safety of local narrowband UVB phototherapy with paint-PUVA in patients with chronic hand eczema of dry and dyshidrotic types unresponsive to conventional therapies.**
Patients/methods: **Fifteen patients (nine men and six women) with chronic hand eczema of dry and dyshidrotic types was included in this prospective, comparative study based on a left to right comparison pattern. The treatments were administered with local narrowband UVB irradiation on one hand and local paint-PUVA using 0.1% 8-methoxypsoralen gel on the other hand three times a week over a 9-week period. The NB-UVB irradiation was administered using a local NB-UVB system equipped with TL-01 lamps. The initial dose was 150 mJ/cm^2 for each patient. An increasing percentile dose schedule based on an increase of 20% was used in every session, until a final dose of 2000 mJ/cm^2 was reached. Evaluation of clinical scores was carried out every 3 weeks during the treatment period.**
Results: **Twelve of the 15 recruited patients completed the study. There was a statistically significant decrease in the mean clinical score at the third, sixth and nineth week in both groups. The difference in clinical response between the two treatment modalities was not statistically significant at the end of the 9-week treatment period. In the narrowband UVB-treated side, the tolerance of all the patients to the treatment was good all patients well-tolerated the treatment with the exception of mild xerosis that responded to topical emollients.**
Conclusion: **Local narrowband UVB phototherapy regimen is as effective as paint-PUVA therapy in patients with chronic hand eczema of dry and dyshidrotic types.**

Key words: **hand eczema; local PUVA; narrowband UVB; treatment.**

Hand eczema is a skin disease characterized by itchy, erythematous and scaly lesions often with a long lasting and relapsing course. The condition is usually resistant to conventional topical therapies such as corticosteroids, anthralin and keratolytics.

Since the late 1980s, the use of narrowband (311 ± 2 nm bandwidth) ultraviolet (UV) B (NB-UVB) lamps has been recognized as an alternative treatment to either broadband UVB (BB-UVB) or psoralen plus UVA (PUVA) (1, 2). In recent studies, NB-UVB irradiation has been shown to reduce the viability and antigen presentation function of Langerhans cells (LCs), as well as induce the secretion of anti-inflammatory cytokins and T-cell apoptosis, the mechanisms that contribute to the pathogenesis and inhibition of contact hypersensitivity (3–7). NB-UVB phototherapy has also been shown to be equally or more effective than BB-UVB or PUVA therapies in eczematous conditions like atopic eczema (8). Although clinical trials demonstrating the efficacy of local PUVA and BB-UVB therapies in the treatment of chronic hand eczema exists, little is known about the efficacy of local NB-UVB phototherapy in this condition (9–11).

The purpose of our study was to investigate the efficacy and safety of local NB-UVB phototherapy in patients with recalcitrant chronic hand eczema of dry and dyshidrotic types.

Patient and methods

Subjects

The study group consisted of 15 patients (nine men and six women, aged between 18 and 73 years). The disease duration ranged from 6 months to 14 years. The inclusion criteria required a diagnosis of biopsy proven chronic hand eczema of dry and dyshidrotic types of more than 4-month duration in which conventional therapies, including topical and oral corticosteroids, topical anthralin, tar, pimecrolimus and emollients, proved ineffective.

Exclusion criteria included a diagnosis of hyperkeratotic hand eczema, topical treatment with corticosteroids within 2 weeks or systemic treatment with corticosteroids or other immunosuppressive agents within the last 4 weeks, unilateral disease, pregnancy, and the inability to meet for follow-up consultations.

The study was approved by the local ethics committee and the patients gave written informed consent before enrolment.

Methods

This investigation was designed as a randomized, controlled, prospective study based on a left to right comparison pattern. The NB-UVB and PUVA treatments were randomly assigned to the left or right hand. The hand treated was selected using a computer-based program, and the treatment was applied three times a week over a 9-week-period.

The NB-UVB irradiation was administered using a local NB-UVB system equipped with Philips TL-01 lamps (Daavlin, M Series, Bryan, OH, USA). The initial dose was 150 mJ/cm^2 for each patient. An increasing percentile dose schedule based on an increase of 20% was used in every session, until a final dose of 2000 mJ/cm^2 was reached.

The UVA irradiation was administered using a local UVA system (Daavlin). The initial dose of psoralen plus UVA irradiation was 1.0 J/cm^2 with an increase of 0.5 J/cm^2 in every second session until a final dose of 7.5 J/cm^2 was achieved. The hand treated with PUVA regimen was painted with 0.1% 8-methoxypsoralen (MOP) in a hydrophilic water/oil emulsion (Vitpso 0.1% gel, Orva pharmaceuticals, Izmir, Turkey), 15 min before the UVA exposure. All patients were advised to wash the hands painted with 8-MOP after the session. Only topical emollients were allowed between treatment sessions. Eye shielding was employed during the irradiation procedure.

Colour photographs were taken before treatment and at the end of the 9-week treatment period.

Clinical evaluation

Clinical assessments were performed by the same investigator (E. S.) every 3 weeks during the 9-week treatment period. The following criteria were evaluated: erythema, squamation, induration, fissures and itching. Each criteria was assessed on a four-point scale: 0, none; 1, mild; 2, moderate; and 3, severe. The total clinical score was calculated by the sum of each variable.

Complete clearance was defined for the patients who achieved a total clinical score of zero at the end of the treatment, and marked clinical improvement was defined for the patients with a reduction of 70% or more with respect to the baseline scores at 9 weeks.

Statistical analysis

Assessment of statistical significance of mean total clinical-score changes within both treated sides was performed on the basis of *t*-test for independent samples. Time courses of the clinical scores for NB-UVB and PUVA groups were plotted according to the Friedman test and Wilcoxon signed test. Significance was defined as $P<0.05$.

Follow-up

The patients who had completed the treatment sessions were evaluated 10 weeks after the last therapy. The severity of relapse was classified as either severe (>70% of pre treatment scores), moderate (30–70% of pre treatment scores), or mild (<30% of pre treatment scores). The patients without an increase in post treatment total clinical scores at the evaluation of follow-up visits were determined to be relapse-free.

Results

Treatment outcome

Twelve of the original 15 patients completed the study. Nine patients were diagnosed as chronic hand eczema of dry type and three patients were diagnosed as chronic hand eczema of dyshidrotic type. There were three drop-outs; one due to treatment failure and two due to non-compliance.

There was no significant difference in total clinical scores between the two treatment modalities with respect to the baseline assessments ($t = 0.604$, $P = 0.552$, *t*-test for independent samples).

Improvement in the total clinical scores was achieved in both treatments at third, sixth and nineth week (Figs 1 and 2). The mean severity scores for the two treatment sides at each visit are shown in Table 1.

There was no significant difference in clinical response between NB-UVB and paint-PUVA treated

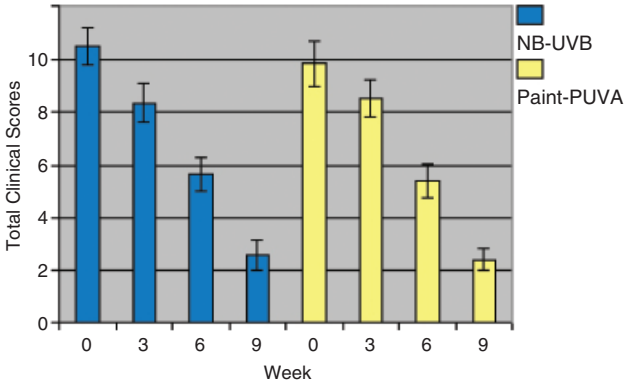

Fig. 1. Effects of localized narrow band-ultraviolet B (NB-UVB) phototherapy and psoralen plus UVA (PUVA) in chronic hand eczema. A significant decrease in mean total clinical scores was achieved on palms receiving either NB-UVB ($P = 0.002$) or PUVA ($P = 0.002$) irradiation at 9 weeks (Wilcoxon's signed test).

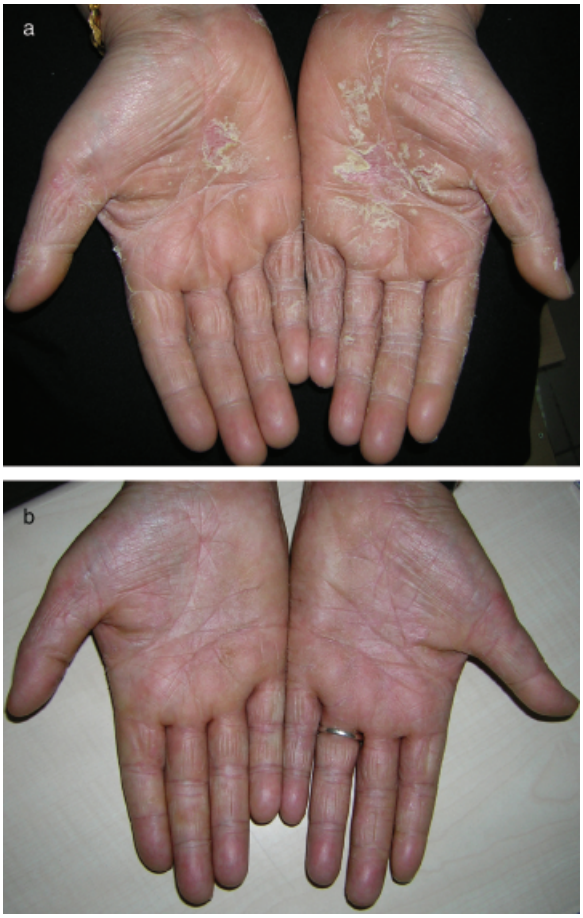

Fig. 2. (*a*) Chronic hand eczema before treatment. (*b*) Marked improvement of the lesions with both local narrowband UVB phototherapy (left hand) and paint-PUVA (right hand) at the end of 9-week treatment period.

Table 1. Mean total clinical scores in each treatment

	NB-UVB-treated side ($n = 12$)		Paint-PUVA-treated side ($n = 12$)	
	Mean total clinical scores	*P* value	Mean total clinical scores	*P* value
Baseline	10.50 ± 2.43		9.83 ± 2.95	
Week 3	8.33 ± 2.53	0.002*	8.50 ± 2.39	0.014*
Week 6	5.67 ± 2.23	0.002*	5.42 ± 2.19	0.002*
Week 9	2.58 ± 2.11	0.002*	2.42 ± 1.44	0.002*

*$P < 0.05$ significant when compared to baseline values (Wilcoxon's signed test).
NB-UVB, narrow band-ultraviolet B; PUVA, psoralen plus ultraviolet A.

sides at nineth week with the percentage reduction in total clinical scores with NB-UVB treated side being 75.43% compared with 75.48% with paint-PUVA treated side ($t = 0.226$, $P = 0.823$, *t*-test for independent samples).

In the NB-UVB phototherapy treated side ($n = 12$), two patients (17%) cleared, nine patients (75%) showed marked clinical improvement and neither clearance nor marked clinical improvement was detected in one patients (8%). In the PUVA-treated side ($n = 12$), one patient (8%) cleared, nine patient (75%) showed marked clinical improvement and neither clearance nor marked clinical improvement was detected in two patients (17%).

During the treatment period, the mean cumulative doses were 34.9 J/cm^2 for the NB-UVB phototherapy, and 111.5 J/cm^2 for the paint-PUVA treatment.

Follow-up

Of the 12 patients in the NB-UVB-treated side who completed the study, eight patients were relapse-free, one had a moderate relapse, and three had a mild relapse. In the paint-PUVA treated side, six patients were relapse-free, one had a severe relapse, one had a moderate relapse and four patients had a mild relapse.

Side effects

No phototoxic reaction or bullous changes were observed in either group. One patient dropped out because of exacerbation of the disease in both hands. In the PUVA group, palmar hyperpigmentation was observed in three cases (25%) which showed slow resolution over time (Fig. 2). In both treatment modalities, mild xerosis that responded to emollients was observed.

Discussion

NB-UVB irradiation has been successfully integrated into the therapeutic approaches of treating atopic

dermatitis and other chronic inflammatory disorders (9). Success in the treatment of eczematous disorders prompted us to examine the effectiveness of local NB-UVB phototherapy in patients with chronic hand eczema.

This study reveals that both local NB-UVB phototherapy and PUVA irradiation show similar beneficial responses. At the end of the treatment period, both NB-UVB and PUVA irradiation provided a statistically significant reduction of total clinical scores, compared with the pre-treatment values. In the study by Rosen et al. (8), patients with chronic eczematous dermatitis of the hands were treated with local BB-UVB phototherapy and oral psoralen plus local UVA (PUVA) photochemotherapy. A statistically significant improvement of mean scores was achieved in both groups, but clinical responses were better in the PUVA treated group. Stege et al. (12) obtained complete remission in seven of 10 patients with local cream PUVA photochemotherapy in patients diagnosed with chronic hand and foot eczema. In another study, treatment of chronic palmoplantar eczema with local bath-PUVA therapy resulted in excellent or good results in 86% of the patients (13). Shephard et al. (14) confirmed in their studies that paint-PUVA using a 0.15% 8-MOP lotion and bath PUVA were equally effective in the treatment of palmoplantar dermatoses including palmoplantar eczema and psoriasis. Our data suggest that local NB-UVB phototherapy is as effective as local paint-PUVA therapy in the treatment of chronic hand eczema of dry and dyshidrotic types. On the other hand, we feel that the clinical improvement in hyperkeratotic hand eczema with local NB-UVB phototherapy may be worse than our results because of diminished penetration of this waveband through thick hyperkeratotic lesions compared with UVA irradiation, thus limiting the use of this treatment modality in hyperkeratotic hand eczema.

The use of NB-UVB phototherapy has increased markedly in recent years and has surpassed the use of PUVA photochemotherapy. NB-UVB is known to interfere with LCs and antigen presentation by reducing the viability and antigen function of LCs (3). In addition, NB-UVB irradiation results in a progressive decline in the expression of the skin-homing molecule cutaneous lymphocyte-associated antigen (CLA), and the non-tissue-specific integrin, very late antigen (VLA), by T lymphocytes (15). The other mechanisms in the inhibition of contact hypersensitivity may be the induction of T-cell apoptosis and the induction of anti-inflammatory and immunosuppressive cytokins (5, 7). NB-UVB irradiation is known to induce production of the anti-inflammatory cytokin interleukin (IL)-10 and decrease the secretion of the proinflammatory cytokines IL-1β, IL-2, IL-5 and IL-6 compared with the pretreatment values (4, 16). In a recent study, NB-UVB has been shown to induce the isomerization of urocanic acid from the *trans* to the *cis* form, which may be important in the immunomodulatory effects for the treatment of skin diseases other than psoriasis (17). UVB-irradiated 1-A^+ LCs and Thy-1^+ dendritic epidermal cells have the potential to deliver down-regulatory signals of contact hypersensitivity in mice (18).

NB-UVB phototherapy has been proven to be more effective than BB-UVB in atopic dermatitis and psoriasis vulgaris (19, 20). NB-UVB also appears to be more immunosuppressive than BB-UVB, which respond to natural killer cell activity and the function of mononuclear cells as measures by lymphoproliferation and cytokine responses (21, 22). This may theoretically explain the better results of NB-UVB in our trial when compared with the study conducted by Rosen et al., which showed the superiority of PUVA therapy over BB-UVB phototherapy in the treatment of chronic hand eczema. To the best of our knowledge, the clinical use of local NB-UVB phototherapy in the treatment of chronic hand eczema has not been published previously, and a standard treatment protocol for this indication does not exist. In our study, the initial dose of NB-UVB irradiation was 150 mJ/cm^2, independent of skin phenotype. Treatment doses were then increased by 20% every session up to 2000 mJ/cm^2. The tolerance of all patients to this regimen was excellent with the exception of mild xerosis that responded to topical emollients. With regards to the total clinical scores, the efficacy of NB-UVB and paint-PUVA were statistically similar at the end of the 9-week treatment period.

Paint-PUVA with 8-MOP has been widely used in the treatment of chronic hand eczema. The psoralen concentrations ranging from 0.0006% to 3% in gel, lotion or cream preparations are applied 15 to 30 min before UVA irradiation (12, 14). The major disadvantage of this regimen is the risk of phototoxicity and pigmentary changes including hyperpigmentation and punctate leukoderma (23, 24). In our trial, phototoxicity was not observed, but three of 12 patients (25%) developed palmar hyperpigmentation that showed a slow resolution over time.

One major concern with the use of NB-UVB phototherapy is the potential carcinogenic risks. In animal studies it has been estimated that the cancer risk of NB-UVB treatment should not be greater than BB-UVB, and, likely, less than PUVA (25, 26). In a recent report, data obtained from 1908 patients trea-

ted with NB-UVB revealed no significant increase in squamous cell carcinoma or malignant melanoma, but a small but statistically significant increase of basal cell carcinoma was detected (27).

In conclusion, we consider that local NB-UVB phototherapy is an effective treatment option in chronic hand eczema of dry and dyshidrotic types.

References

1. Green C, Ferguson J, Lakshmipathi T, Johnson BE. 311 nm UVB phototherapy – an effective treatment for psoriasis. Br J Dermatol 1988; **119:** 691–696.
2. Larko O. Treatment of psoriasis with a new UVB-lamp. Acta Derm Venereol 1989; **69:** 357–359.
3. Kolgen W, Both H, van Weelden H, et al. Epidermal langerhans cell depletion after artificial ultraviolet B irradiation of human skin *in vivo*: apoptosis versus migration. J Invest Dermatol 2002; **118:** 812–817.
4. Sigmundsdottir H, Johnston A, Gudjonsson JE, Valdimarsson H. Narrowband-UVB irradiation decreases the production of pro-inflammatory cytokines by stimulated T cells. Arch Dermatol Res 2005; **297:** 39–42.
5. Krutmann J, Morita A. Mechanisms of ultraviolet (UV) B and UVA phototherapy. J Investig Dermatol Symp Proc 1999; **4:** 70–72.
6. Beissert S, Schwarz T. Role of immunomodulation in diseases responsive to phototherapy. Methods 2002; **28:** 138–144.
7. Walters IB, Ozawa M, Cardinale I, et al. Narrowband (312-nm) UV-B suppresses interferon gamma and interleukin (IL) 12 and increases IL-4 transcripts: differential regulation of cytokines at the single-cell level. Arch Dermatol 2003; **139:** 155–161.
8. Rosen K, Mobacken H, Swanbeck G. Chronic eczematous dermatitis of the hands: a comparison of PUVA and UVB treatment. Acta Derm Venereol 1987; **67:** 48–54.
9. Ibbotson SH, Bilsland D, Cox NH, et al. An update and guidance on narrowband ultraviolet B phototherapy: a British photodermatology group workshop report. Br J Dermatol 2004; **151:** 283–297.
10. Behrens S, von Kobyletzki G, Gruss C, et al. PUVA-bath photochemotherapy (PUVA-soak therapy) of recalcitrant dermatoses of the palms and soles. Photodermatol Photoimmunol Photomed 1999; **15:** 47–51.
11. Hawk JL, Grice PL. The efficacy of localized PUVA therapy for chronic hand and foot dermatoses. Clin Exp Dermatol 1994; **19:** 479–482.
12. Stege H, Berneburg M, Ruzicka T, Krutmann J. Cream PUVA photochemotherapy. Hautarzt 1997; **48:** 89–93.
13. Schempp CM, Muller H, Czech W, Schopf E, Simon JC. Treatment of chronic palmoplantar eczema with local bath-PUVA therapy. J Am Acad Dermatol 1997; **36:** 733–737.
14. Shephard SE, Schregenberger N, Dummer R, Panizzon RG. Comparison of 8-MOP aqueous bath and 8-MOP ethanolic lotion (Meladinine) in local PUVA therapy. Dermatology 1998; **197:** 25–30.
15. Sigmundsdottir H, Gudjohnsson JE, Valdimarsson H. The effects of ultraviolet B treatment on the expression of adhesion molecules by circulating T lymphocytes in psoriasis. Br J Dermatol 2003; **148:** 996–1000.
16. Piskin G, Bos JD, Teunissen MB. Neutrophils infiltrating ultraviolet B-irradiated normal human skin display high IL-10 expression. Arch Dermatol Res 2005; **296:** 339–342.
17. Gilmour JW, Vestey JP, George S, Norval M. Effect of phototherapy and urocanic acid isomers on natural killer cell function. J Invest Dermatol 1993; **101:** 169–174.
18. Cruz PD Jr, Nixon-Fulton J, Tigelaar RE, Bergstresser PR. Disparate effects of *in vitro* low-dose UVB irradiation on intravenous immunization with purified epidermal cell subpopulations for the induction of contact hypersensitivity. J Invest Dermatol 1989; **92:** 160–165.
19. Reynolds NJ, Franklin V, Gray JC, Diffey BL, Farr PM. Narrow-band ultraviolet B and broad-band ultraviolet A phototherapy in adult atopic eczema: a randomised controlled trial. Lancet 2001; **357:** 2012–2016.
20. Coven TR, Burack LH, Gilleaudeau R, et al. Narrowband UV-B produces superior clinical and histopathological resolution of moderate-to-severe psoriasis in patients compared with broad-band UV-B. Arch Dermatol 1997; **133:** 1514–1522.
21. 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.
22. Diffey BL. Factors affecting the choice of a ceiling on the number of exposures with TL01 ultraviolet B phototherapy. Br J Dermatol 2003; **149:** 428–430.
23. Takashima A, Yamamoto K, Kimura S, Takakuwa Y, Mizuno N. Allergic contact and photocontact dermatitis due to psoralens in patients with psoriasis treated with topical PUVA. Br J Dermatol 1991; **124:** 37–42.
24. Park JH, Lee MH. Case of leukoderma punctata after topical PUVA treatment. Int J Dermatol 2004; **43:** 138–139.
25. Flindt-Hansen H, McFadden N, Eeg-Larsen T, Thune P. Effect of a new narrow-band UVB lamp on photocarcinogenesis in mice. Acta Derm Venereol 1991; **71:** 245–248.
26. Gibbs NK, Traynor NJ, MacKie RM, et al. The phototumorigenic potential of broad-band (270–350 nm) and narrow-band (311–313 nm) phototherapy sources cannot be predicted by their edematogenic potential in hairless mouse skin. J Invest Dermatol 1995; **104:** 359–363.
27. Man I, Crombie IK, Dawe RS, Ibbotson SH, Ferguson J. The photocarcinogenic risk of narrowband UVB (TL-01) phototherapy: early follow-up data. Br J Dermatol 2005; **152:** 755–757.

Accepted for publication 01 September 2006

Corresponding author:
Engin Sezer, M.D.
Gaziosmanpasa Universitesi Hastanesi
Dermatoloji Anabilim Dali
Tokat 60100
Turkey
Tel: +90 (538) 5660448
Fax: +90 (356) 2129417
e-mail: eseze@yahoo.com