

THERAPEUTIC HOTLINE

Treatment of moderate and severe adult chronic atopic dermatitis with narrow-band UVB and the combination of narrow-band UVB/UVA phototherapy

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ABSTRACT: The phototherapy is a safe and effective technique for the treatment of adult patients with atopic dermatitis (AD). The treatment of chronic forms of the disease is most often done with narrow-band UVB (NB-UVB). There also exist effective phototherapy options against the AD. The aim of this study was to assess if the combination of NB-UVB with UVA was more effective than the treatment with only NB-UVB against adult chronic AD. We carried out a prospective and observational study. Adult patients with chronic AD with more than 50% of the total body surface area affected (TBSA) were included. The affected TBSA was calculated using the so-called “rule of nines.” Patients with a clearance rate >75% of the initial affected TBSA or complete clearance rate were considered as complete response (CR). An analogue scale from 0 to 10 was used to measure the improvement grade of the pruritus. The treatments were repeated three times a week. The initial doses of NB-UVB and UVA were determined by patient's phototype. The treatments were performed using a phototherapy booth (UV7002, Walmann, Villingen-Schwenningen, Germany®) with TL01 and UVA fluorescent lamps. Statistical analysis was performed with SPSS® (IBM, New York, NY) for Windows 21.0. A total of 26 patients with adult chronic AD were included in the study, 16 patients were treated with UVB-BE and 10 patients with the combined treatment option NB-UVB/UVA. The mean value of cumulative doses and the mean number of performed treatments were similar between both groups of patients ($p > 0.05$). The mean value of duration of response was significantly higher in the patients treated only with NB-UVB, 101 versus 6.8 months ($p \geq 0.05$). No differences were observed for the patients that showed complete response ($p = 0.42$) and in the analogue scale of pruritus ($p > 0.005$). In our study, the patients treated with the combination of NB-UVB and UVA were similar to the patient that were only treated with NB-UVB e. Further prospective and controlled studies have to be performed in order to determine the dosing regimens of phototherapy in adult patients with AD.

KEYWORDS: atopic dermatitis, phototherapy, treatment

Introduction

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The phototherapy is a safe and effective technique for the treatment of adult patients with atopic dermatitis (AD). Various forms of

phototherapy have been shown to be useful for the treatment of chronic, pruritic and lichenified AD in adult patients, including broad-band (BB) UVB (280–315 nm), narrow-band (NB) UVB (311–313 nm), UVA (315–400 nm), UVA1 (340–400 nm), full spectrum light (FSL, 320–5000 nm), monochromatic excimer light (308 nm), and psoralen and ultraviolet light (PUVA) (1,2). In general, phototherapy is not indicated in acute stages of AD. Based on results of different studies and guidelines, NB-UVB is preferred to BB-UVB because is less erythematogenic (3). The efficacy of UVA1 applied in moderate doses was similar to the efficacy of NB-UVB (4). High doses of UVA1 were effective in control flare-ups and severe Ads (5,6). It has been recently demonstrated that PUVA provide a better short and long-term response with a lower number of treatment sessions than medium-dose UVA1 (7). PUVA is not recommended as a first-line phototherapy treatment option against AD (3). PUVA can be performed when other phototherapy treatment options have failed. New devices as the 308 nm excimer laser or FSL have to be considered although they have not been properly assessed for AD (3).

The AD is most common in children than in adults and in the last years, only few studies have been published concerning the option of treatment of adult AD with phototherapy. The aim of this study was to compare the efficacy of the treatment with only NB-UVB with the combination of NB-UVB/UVA (broad-band UVA as used in psoralen photochemotherapy) as an additional second-line e therapy for adult patients with moderate and severe chronic AD. Medium to high doses of UVA1 are effective against AD but it requires special irradiation devices which are only available in specialist centers. Little is known about the efficacy of the combined therapy option UVB/UVA, but not NB-UVB (5,8).

Material and methods

The study was performed as a prospective, open and observational trial. The data of adult patients treated against AD was collected between November 2011 and March 2014. Following patients were included in this study: patients with more than the 50% of the total body surface area (TBSA) affected, with no response to topical treatment and oral corticoids, and patients with eczema (present at least for

one month). Age, sex, skin type, clinical form (lichenified eczema or prurigo) of the AD, treatment, number of sessions, cumulative dose, and response data were collected. The affected TBSA was calculated using the classical “rule of nines”. Patients with a clearance rate >75% of the initial affected TBSA or complete clearance rate were considered as complete response (CR). Adults with a clearance rate <75% were classified as incomplete response (IR). Follow-up of all patients with CR was performed and a exacerbation >25% of the TBSA was considered a relapse. The duration of the response in patients with CR was also measured. Concomitant treatments and adverse effects were also collected. An analogue scale from 0 to 10 was used to measure the grade of improvement of the pruritus. All patients were treated three times a week. All patients were selected randomly for each treatment. The initial doses of NB-UVB and UVA were determined by the patient skin phototype (2). The dose of irradiation was increased by 10% in patients treated with UVB BE that did not present erythema. If symptomatic erythema appeared, the irradiation dose was reduced to 20%. The increase of the irradiation dose in patients also treated with UVA was determined by the patient skin type (0.5 J/cm² for skin type I-II, and 1 J/cm² for skin type III-IV) and similarly to the dosing of UVA radiation for oral psoralen and ultraviolet light A². Treatment was performed using a phototherapy booth (UV7002, Walmann®) with TL01 and UVA fluorescent lamps which allowed use NB-UVB as monotherapy or in combination with UVA. The emission spectrum had a meannwavelength of 313 nm for NB-UVB (310–315 nm) and a range of 320–410 nm for UVA. Therapy was performed under the supervision of a dermatologist and executed by dermatology nurse specialists trained in phototherapy. All patients wore UV-blocking goggles and their genitals were covered to avoid pain induced by from UV exposure.

Statistical analysis was performed with SPSS® for Windows 21.0. The primary outcome measure of the study was the reduction of TBSA. Secondary outcome measures were the length of remission after treatment and the number of sessions performed. The null hypothesis was based on the assumption that there is no significant difference between both treatment options. The Chi-squared test was performed to determine the homogeneity in the compared two groups and the Z test was used to determine the difference between the two treatments modalities for

Table 1. Characteristics of patients with adult AD treated with NB-UVB and NB-UVB/UVA

Characteristics	NB-UVB	NBUVB/UVA	<i>p</i> -values
Number of patients	16	10	
Sex (F/M)	6/10	7/3	$p = 0.22^{\chi}$
Age	34,88	46,4	$p = 0.156^Z$
Clinical form (lichenified/prurigo)	12/4	8/2	$p = 0,768^{\chi Z}$
Skin type (I-II/III-IV)	5/11	7/3	$p = 0.054^{\chi}$
Mean TBSA affected	56%	65%	$p = 0.857^Z$
Mean value of cumulative dose	8.93	8,23 + 16,63	$p = 0.222^Z$
Mean number of treatments	19.93	19,3	$p = 0.08^Z$
Mean value for the duration of response (months)	10.1	6.8	$p \geq 0.05^U$
Complete response	11	5	$p = 0.42^F$
Erythema	2	0	$p > 0.05^U$
Analogue scale of pruritus	6	6	$p > 0.05^U$
Treatment dropout	2	0	

χ , Chi cuadrado test; Z , Z-test; U , U Mann Whitney test.

continuous data. The Mann–Whitney U test was used to calculate the duration of the response. Additionally, the Fisher test was used to compare the number of patients reaching the predefined outcome variable (reduction $>75\%$ of initial TBSA). All given p -values are two-tailed and $p > 0.05$ indicates statistical significance.

Results

Twenty six patients with adult chronic AD were included in this study, 20 with lichenified eczema and 6 with prurigo eczema. The characteristics of the patients are summarized in Table 1. Sixteen patients were treated with UVB-BE and 10 patients with the combined treatment option NB-UVB/UVA (see Figure 1). All patients who received UVA irradiation in combination with UVB-NB were selected randomly. Among the 16 patients treated with NB-UVB, 6 were females and 10 were males. Almost all the patients presented lichenified eczemas (12 vs. 4 with prurigo eczema) with a mean age of 34.88 years. Conversely, most of the patients treated with the combination of NB-UVB and UVA were males ($p = 0.22$), also with a predominance of lichenified forms (8 vs. 2, $p > 0.05$) with a mean age of 46.40 ($p = 0.152$). Most of the patients treated belonged to the II to IV skin type groups ($p = 0.054$) with an affected TBSA mean value of

**FIG. 1.** Image of a patient before (A) and after (B) the treatment with NB-UVB (number of sessions or number of treatments = 20).

56% and 63%, respectively (NB-UVB vs. NB-UVB/UVA, $p = 0.857$). The mean value of cumulative doses of UVB and the mean number of performed sessions were similar between both groups of patients ($p > 0.05$). The mean value for the duration of the response was significantly higher in patients treated only with NB-UVB, 10.1 versus 6.8 ($p \geq 0.05$). No significant differences were observed when complete response rates were analyzed ($p = 0.42$). No adverse effects were observed in patients treated with the combined treatment option. Nevertheless, two patients treated with NB-UVB suffered erythema and at this point, treatment was ended. No differences were found when the analogue scale of pruritus was analyzed.

Discussion

Several studies have shown beneficial effects of phototherapy in AD. The reasons for the efficacy of this treatment option are following: first, phototherapy induces immunosuppressive responses, including apoptosis of inflammatory T-cells, inhibition of Langerhans cells antigen-presenting function and reduction of the production of type 1 cytokine. In addition, UV radiation reduces the colonization of *S. aureus* and *Pityrosporum orbiculare*. Furthermore, UV induces the swelling of the stratum corneum improving the skin barrier and reducing the penetration of antigens (1,2).

We present here a prospective study with few limitations as the absence of a control group and a small number of patients treated. Maybe an intra-patient comparison would be controlled these limitations but in was not possible in the booth used. 11 of 16 (69%) of our patients achieved complete response after treatment with NB-UVB and 5 of 10 (50%) of the patients showed complete response with the combined

Table 2. Phototherapy Studies Published for the Treatment Of Atopic Dermatitis With UVB, UVA, UVA1 or the combined treatment form NB-UVB/UVA

Author/Year	N	Intervention	Results
Jeckler, 1990 (8)	39	UVB versus UVAB 8 week	Superiority of UVAB in total score and pruritus ($p < 0.05$)
Jeckler 1991 (9)	33	UVB versus UVA 8 week	Superiority of UVA in score and pruritus ($p < 0.02$)
Jeckler, 1991 (10)	20/28	20: low doses UVB versus UVAB 28: UVA versus UVAB	Superiority of UVAB ($p < 0.05$) No differences in pruritus
Der-Petrossian (11)	12	NB-UVB versus Bath-PUVA Chronic forms of AD 8 weeks	No differences ($p > 0.05$)
Reynolds, 2001 (12)	73	NB-UVB versus UVA MD Adult chronic forms of AD 12 weeks	Superiority of NB-UVB in reduction and maintenance
Legat, 2003 (13)	9	NB-UVB versus UVA1 MD Chronic forms 8 weeks	Superiority of NB-UVB in score and pruritus ($p < 0.05$)
Majoie, 2009 (4)	13	NB-UVB versus UVA1 MD 8 weeks	No differences in score and pruritus ($p > 0.05$)
Gamblicher, 2009 (14)	47	NB-UVB versus UVA1 MD	No differences in score and pruritus ($p > 0.05$)
Present study	26	NB-UVB versus NB-UVB+UVA Adult chronic forms of AD	No differences in BSA and pruritus ($p > 0.02$)

AD, atopic dermatitis; MD, medium doses.

option of treatment. No significant differences were observed between patients that showed complete responses ($p = 0.42$). These results confirm previous reports concerning the efficacy of NB-UVB in adult AD (67% with complete response) (4,11–14) and suggest that the addition of UVA to NB-UVB did not produce any benefit/did not have beneficial results. A study where adult AD was treated only with UVA showed that the 32% of the patients achieved complete response (10), but surprisingly, when UVA was combined with NB-UVB, the efficacy of NB-UVB did not improve in our group of patients. No significant differences were observed when pruritus and adverse effects were compared for both treatment options.

In the last years, only a few studies were published concerning adult AD. These studies compared broad-band or narrow-band UVB and other phototherapy treatment options. The data of these studies is summarized in the Table 2. The most recent studies demonstrate that NB-UVB (4,11–14), is the most efficient treatment option against AD, including pruritus control (medium doses of UVA1, Bath-PUVA or medium doses of broad-band UVA). The study of Reynolds et al. (12) published in 2001, was performed with 72 patients with adult chronic AD. This is the biggest study assessing NB-UVB in AD. The authors com-

pared the efficacy of NB-UVB with broad-band UVA and concluded that NB-UVB was more effective. Nevertheless, it is difficult to compare the results of different studies because some of them analyzed different parameters, such as exacerbation or chronic forms, and some of them were executed with adult patients, or children and some studies compared both of them. AD has a seasonal influence and the dosage regimens are not standardized (1,2).

It can be proposed the combination of UVA1 in medium doses and NB-UVB as the ideal phototherapy option for AD (1). However, UVA1 requires and special device whereas the combination of UVA and NB-UVB is available in the same booth (1,15). The proper selection of the patients treated with the combined treatment form of UVB-BE/UVA could improve the results obtained for this study. All patients were randomized and showed a chronic AD (duration at least of one month). It can be also suggested that the combination with UVA is more suitable and achieve better results in patients with subacute flares where UVA1 is more effective. However, doses of UVA (no UVA1) are not optimized for the treatment of AD (1,5,10).

Severe adult chronic AD is an unusual skin disease. Nowadays, there is no consensus to choose the best treatment option. The classification of eczema is difficult, and several scales

have been published. The Six area, six sign AD (SASSAD), (15) the patient oriented eczema measure (POEM) (16) and the children's dermatology life quality index (CDLQI) (17) are well-described and validated as scoring systems/for eczema. That is not the case for the psoriasis area severity index (PASI) in psoriasis; clinical trials performed in patients with eczema used different scoring systems making direct comparison impossible. Recently, in the same way as PASI for psoriasis, the scoring AD (SCORAD) 75 (18) has been proposed by the European Task Force on AD (ETFAD) as a better evaluation tool to assess the severity of AD. We also measured the TBSA and subjective pruritus after treatment. However, clinical symptoms of disease as for example exudation, excoriation, dryness or erythema should have been taken into account. The lack of a universal metric system of the severity of AD is the main limitation in the reviewed studies.

The optimal doses of phototherapy in adult atopic dermatosis are still not defined. Data from adult patients with psoriasis showed that psoriasis was effectively cleared with doses close to MED values. However, it is not defined, if patients with eczema respond preferentially to low or high dose regimens. The mean value of the initial dose, the cumulative dose and number of treatments was similar between both groups, but the duration of response in patients treated only with NB-UVB was higher (10.1 months vs. 6.8 months, $p < 0.05$). We did not find any explanation for this result, but maybe the addition of UVA decrease the time of clearance or other parameters such as the treatment compliance and the skin care after the treatment influence the therapy. A moderate and/or severe eczema that persists in adulthood is inherently more resistant to the/its treatment. In our study, we show that NB-UVB is an alternative option for the treatment of chronic dermatitis with moderate results. The combination with UVA did not show any benefits. Further prospective and controlled studies have to be performed in order to determine the dosing regimens, the best way to select the patients, the response rates and to maximize the efficacy of phototherapy in adult AD.

References

1. Garritsen FM, Brouwer MW, Limpens J, Spuls PI. Photo (chemo)therapy in the management of atopic dermatitis: an updated systematic review with the use of GRADE and implications for practice and research. *Br J Dermatol* 2013; **170**: 501–513.
2. Sidbury R, Davis D, Cohen D, et al. Guidelines of care for the management of atopic dermatitis. Section 3. Management and treatment with phototherapy and systemic agents. *J Am Acad Dermatol* 2014; **71**: 1218–1233.
3. Ring J, Alomar A, Bieber T, et al. Guidelines for treatment of atopic eczema (atopic dermatitis). Part II. *J Eur Acad Dermatol* 2012; **26**: 1176–1193.
4. Majoie IM, Oldhoff JM, van Weelden H, et al. Narrow-band UVB and medium-dose of UVA1 are equally effective in the treatment of moderate to severe atopic dermatitis. *J Am Acad Dermatol* 2009; **60**: 70–84.
5. Krutmann J, Diepgen T, Luger T, et al. High-dose UVA1 therapy for atopic dermatitis: results of amulticenter trial. *J Am Acad Dermatol* 1998; **38**: 589–593.
6. Gambichler T, Terra S, Kreuter A. Treatments regimens, protocols, dosage, and indications for UVA1 phototherapy: facts and controversies. *Clin Dermatol* 2013; **31**: 438–454.
7. Tzaneva S, Kittler H, Holzer G, et al. 5-methoxypsoralen plus ultraviolet (UV) A is superior to medium-dose UVA1 in the treatment of severe atopic dermatitis. A randomized crossover trial. *Br J Dermatol* 2010; **162**: 655–660.
8. Jekler J, Larko O. Combined UVA-UVB versus UVB phototherapy for atopic dermatitis: a paired combination study. *J Am Acad Dermatol* 1990; **22**: 49–53.
9. Jekler J, Larko O. UVA solarium versus UVB phototherapy of atopic dermatitis: a paired comparison study. *Br J Dermatol* 1991; **125**: 569–572.
10. Jekler J, Larko O. Phototherapy for atopic dermatitis with ultraviolet A (UVA), low-dose UVB and combined UVA and UVB: two paired-comparison studies. *Photodermatol Photoimmunol Photomed* 1991; **8**: 151–156.
11. Der-Petrossian M, Seeber A, Honigsmann H, Tanew A. Half-side comparison study on the efficacy of 8-methoxypsoralen bath-PUVA versus narrow-band ultraviolet B phototherapy in patients with severe chronic atopic dermatitis. *Br J Dermatol* 2000; **142**: 39–43.
12. Reynolds NJ, Franklin V, Gray JC, Diffey BL, Farr PM. Narrow-band ultraviolet B and broad-band ultraviolet A phototherapy in adult chronic atopic eczema: A randomized controlled trial. *Lancet* 2001; **357**: 2012–2016.
13. Legat FJ, Hofer A, Brabek E, Quehen beger F, Kerl H, Wolf P. Narrowband-UVB vs medium-dose UVA-1 phototherapy in chronic atopic dermatitis. *Arch Dermatol* 2003; **139**: 223–224.
14. Gambichler T, Othlinghaus N, Tomi NS, et al. Medium-dose ultraviolet (UV) A1 vs narrow-band UVB phototherapy in atopic eczema: a randomized crossover study. *Br J Dermatol* 2009; **160**: 652–658.
15. Carrascosa JM, Gardeazabal J, Pérez-Feirrols A. Consensus document on phototherapy: PUVA therapy and narrow-band UVB therapy. *Actas Dermosifiliog* 2005; **96**: 635–658.
16. Charman CR, Venn AJ, Williams HC. The Patient-Oriented Eczema Measure. *Arch Dermatol* 2004; **140**: 1513–1519.
17. Lewis-Jones MS, Finlay AY. The CDLQI: initial validation and practical use. *Br J Dermatol* 1998; **138**: 107–113.
18. Harari M, Dreier J, Czarnowicki T, Ruzicka T, Ingber A. SCORAD 75: a new metric for assessing treatment outcomes in atopic dermatitis. *J Eur Acad Dermatol* 2012; **26**: 1510–1515.