

Itch Relief in Atopic Dermatitis: Comparison of Narrowband Ultraviolet B Radiation and Cyclosporine Treatment

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Atopic dermatitis (AD) is the most common itchy inflammatory skin disease with a chronic and recurrent course worldwide (1). According to the latest treatment consensus for management of AD, there is a variety of therapeutic methods that can be used in patients with AD, including narrowband ultraviolet B radiation (NB-UVB) and systemic immunomodulating therapy for patients with more severe AD. However, studies dealing specifically with itch improvement in subjects with AD are very limited (1). The aims of this study were to evaluate and compare itch response in patients with AD treated with NB-UVB and cyclosporine (CsA).

PATIENTS AND METHODS

The study was conducted over the last 2 years (14 months). It was approved by the Bioethics Committee of Jagiellonian University (consent number 1072.6120.139.2019) and performed according to the principles of the Declaration of Helsinki.

A group of 42 adult Caucasian patients with moderate-to-severe, childhood onset, chronic AD, based on the criteria of Hanifin & Rajka (2), were recruited into the study. Exclusion criteria were: lack of consent to participation, age below 18 years, comorbid pruritic cutaneous and systemic disorders. All unrelated causes of insomnia (psychological and somatic) were also excluded. The wash-out period for systemic immunosuppressive agents and sleeping medications was at least 2 months and for any type of phototherapy at least 6 months before study recruitment. Any recent use (within the previous 4 weeks) of systemic antipruritic agents, topical corticosteroids and calcineurin inhibitors was not allowed. Subjects were allowed to apply previously used emollients 2–3 times per day. A total of 21 patients with AD were put on NB-UVB therapy and 21 patients with AD received CsA treatment. Phototherapy was performed using the stand-up cubicle Cosmedico GP-42 (Cosmedico Medizintechnik GmbH, VS-Schwenningen, Germany) cabin with TL 100W/01 fluorescent lamps (Philips, Eindhoven, The Netherlands). Patients undergoing NB-UVB therapy represented phototypes II and III; the initial radiation doses were 0.22 and 0.26 J/cm², respectively. The patients were irradiated 3 times a week and the radiation dose was modified by 0.025–0.04 J/cm² every second session, until erythema appeared. The maximum dose of NB-UVB radiation was 0.56 J/cm². The baseline dose of CsA was 3.5 mg/kg/day in 2 divided doses, and the dose was increased after 2 weeks of therapy. The maximum dose of CsA administered was 5 mg/kg/day. All patients were allowed to use topical emollients during the whole study period. Both treatment groups continued therapy for 12 weeks.

All assessments were performed by the same dermatologist (AKJ) at the baseline visit and at week 12 of the study. The worst itch during last 24 h was evaluated with a visual analogue scale (Worst Itch Visual Analogue Scale; WI-VAS) (3). The severity of skin lesions was assessed with the Eczema Area and Severity

Index (EASI) (4), quality of life with the Dermatology Life Quality Index (DLQI) (5) and quality of sleep with the Athens Insomnia Scale (AIS) (6). The safety profile of both treatment modalities was also evaluated according to latest European recommendations.

Statistical analyses were performed using Statistica 12 software (StatSoft, Tulsa, OK, USA) with appropriate tests (Mann–Whitney *U* test, Pearson's χ^2 test and Wilcoxon signed-rank test). The level of significance was set at α 0.05.

RESULTS

The baseline characteristics of both studied groups showed no significant difference in itch intensity (WI-VAS) ($p=0.71$), disease severity (EASI) ($p=0.27$), quality of life (DLQI) ($p=0.07$) or sleep disturbance (AIS) ($p=0.67$) between patients treated with NB-UVB and CsA (Table S1¹). NB-UVB resulted in significant ($p<0.0001$) improvement in itch. WI-VAS scores were reduced from 9.4 ± 0.9 to 4.0 ± 1.1 points. A similar phenomenon was observed in patients on CsA; their itch intensity decreased from 9.5 ± 0.8 to 6.9 ± 1.0 points ($p<0.0001$). Comparing both treatment groups, results for itch reduction were significantly better ($p<0.0001$) among patients treated with NB-UVB than those treated with CsA (Table I). In the NB-UVB group itch was reduced by 5.4 points, reaching the minimal clinical important difference (MCID) for itch reduction (7). Of note, MCID was not achieved with CsA treatment (reduction by 2.6 points).

Moreover, there was a difference in the distribution of patients with various itch intensities after treatment (Fig. S1¹). At baseline, the large majority of patients reported very severe itch in both groups (85.7% in the NB-UVB group and 90.5% in the CsA group). After the therapy 95.2% of NB-UVB-treated patients reported itch of moderate intensity, while 52.4% of patients treated with CsA had severe itch (Fig. S1¹).

In addition, in parallel with the improvement in itch intensity, a reduction in EASI scores was observed (Table I). Again, NB-UVB treatment showed significantly ($p=0.03$) better results than CsA treatment. The same was observed for DLQI and AIS scores ($p<0.0001$ for both assessments).

No serious adverse events were reported. Only 2 patients treated with CsA presented with mild hypertension

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Table I. Efficacy of narrow-band ultraviolet B (NB-UVB) and cyclosporine (CsA) treatment for atopic dermatitis

Measure	NB-UVB group			CsA group			
	Baseline Mean ± SD (range)	Week 12 Mean ± SD (range)	p-value	Baseline Mean ± SD (range)	Week 12 Mean ± SD (range)	p-value	p-value
WI-VAS (points)	9.4 ± 0.9 (7–10)	4.0 ± 1.1 (3–7)	<0.0001	9.5 ± 0.8 (7–10)	6.9 ± 1.0 (5–9)	<0.0001	<0.0001
EASI (points)	41.7 ± 6.6 (31.4–49.7)	30.0 ± 9.9 (15.3–46.5)	<0.0001	44.5 ± 4.9 (35.4–49.4)	36.8 ± 4.6 (26.7–43.3)	<0.0001	0.03
DLQI (points)	10.7 ± 2.1 (6–14)	4.9 ± 1.7 (2–7)	<0.0001	12.2 ± 2.5 (8–16)	8.5 ± 2.5 (4–15)	<0.0001	<0.0001
AIS (points)	13.5 ± 2.4 (10–17)	4.0 ± 1.1 (2–7)	<0.0001	13.9 ± 1.8 (11–17)	5.9 ± 0.9 (4–9)	<0.0001	<0.0001

WI-VAS: Worst Itch Visual Analogue Scale; EASI: Eczema Area and Severity Index; DLQI: Dermatology Life Index Quality; AIS: Athens Insomnia Scale; SD: standard deviation.

during the treatment, with no need for a reduction in CsA dose or any intervention to reduce hypertension. One patient treated with CsA experienced headache. NB-UVB treatment was well tolerated.

DISCUSSION

Both NB-UVB and CsA are regarded as effective treatment modalities for AD (1). However, to the best of our knowledge, comparative data on NB-UVB and CsA effectiveness in itch improvement has not been reported to date.

In 2001 Granlund et al. (8) reported a comparison study of CsA and UV-AB phototherapy during a one-year study period in a group of 72 patients. They found that treatment with CsA at the beginning in each cycle of therapy seemed to be more effective than treatment with UV-AB, but after 10 weeks of treatment there were no statistically significant differences in SCORing Atopic Dermatitis (SCORAD) points in the CsA and UV-AB treatment groups.

In Legat et al. (9), a statistically significant reduction in itch VAS score (67%) was observed after 8 weeks of NB-UVB treatment in 9 patients with AD, in contrast to UVA1 treatment (37%). Gambichler et al. (10) demonstrated a relative reduction of 25.2% in itch VAS in patients with AD treated with NB-UVB- (6-week therapy), which was not significantly different from the UVA1-treated group (16.0%). Similarly, Majoie et al. (11), evaluating a limited number of patients with AD (13 subjects), observed a marked improvement in itch in patients with AD on 8 weeks of NB-UVB therapy (VAS scores decreased from 7.0 to 1.8 points). These results are in agreement with the current study, which showed a 42.6% improvement in WI-VAS scores in patients treated with NB-UVB for 12 weeks. Moreover, patients on NB-UVB therapy, similar to those in the study by Majoie et al. (11), reached the MCID level for itch reduction (7).

Concerning the effect of CsA on itch in patients with AD, Wahlgren et al. (12) found that, during 10 days of treatment, itch VAS scores were reduced by more than 50% in a CsA treated group. In contrast, in patients on placebo even higher VAS scores were noted at day 10 of therapy. Otsuka et al. (13), in an uncontrolled study of 16 adult patients with AD, suggested that a low dose of CsA (3 mg/kg/day) might significantly improve itch sensation. They highlighted the rapid effect of CsA on itch reduction, which was observed as early as day 3 of therapy, when

the clinical manifestation of AD remained unchanged. Nakamura et al. (14) showed a decrease in itch VAS scores during CsA treatment, noting that, in some patients, the itch improvement did not correspond with the dose of CsA. Interestingly, in 1 of 10 patients studied itch intensity remained unchanged. In the cohort of CsA-treated patients in the current study itch decreased in all subjects.

Brazelli et al. (15) suggested the possibility of using a sequential combination of NB-UVB and CsA treatments for AD, in order to extend the remission period, and this could be of particular interest in the context of itch in subjects with AD.

This study has several limitations. It was a single-centre study with a relatively limited number of patients, and lacked a follow-up period. Moreover, the study was not blinded, although in our opinion it reflects a real-life situation. The results require confirmation in further studies; however, we believe that these observations could of interest in daily clinical practice.

The authors have no conflicts of interests to declare.

REFERENCES

1. Wollenberg A, Barbarot S, Bieber T, Christen-Zaech S, Deleuran M, Fink-Wagner A, et al. Consensus-based European guidelines for treatment of atopic eczema (atopic dermatitis) in adults and children: part I. *J Eur Acad Dermatol Venereol* 2018; 32: 657–682.
2. Hanifin JM, Rajka G. Diagnostic features of atopic dermatitis. *Acta Derm Venereol* 1980; Suppl 92: 44–47.
3. Schoch D, Sommer R, Augustin M, Ständer S, Blome C. Patient-reported outcome measures in pruritus: a systematic review of measurement properties. *J Invest Dermatol* 2017; 137: 2069–2077.
4. Leshem YA, Hajar T, Hanifin JM, Simpson EL. What the Eczema Area and Severity Index score tells us about the severity of atopic dermatitis: an interpretability study. *Br J Dermatol* 2015; 172: 1353–1357.
5. Finlay AY, Khan GK. Dermatology Life Quality Index (DLQI) – a simple practical measure for routine clinical use. *Clin Exp Dermatol* 1994; 19: 210–216.
6. Soldatos CR, Dikeos DG, Paparrigopoulos TJ. The diagnostic validity of the Athens Insomnia Scale. *J Psychosom Res* 2003; 55: 263–267.
7. Reich A, Riepe C, Anastasiadou Z, Mędrak K, Augustin M, Szepletowski JC, et al. Itch assessment with visual analogue scale and numerical rating scale: determination of minimal clinically important difference in chronic itch. *Acta Derm Venereol* 2016; 96: 978–980.
8. Granlund H, Erkkö P, Remitz A, Langeland T, Helsing P, Nuutinen M, et al. Comparison of cyclosporin and UVAB phototherapy for intermittent one-year treatment of atopic dermatitis. *Acta Derm Venereol* 2001; 81: 22–27.
9. Legat FJ, Hofer A, Brabek E, Quehenberger F, Kerl H, Wolf P.

Narrowband UV-B vs medium-dose UV-A1 phototherapy in chronic atopic dermatitis. *Arch Dermatol* 2003; 139: 223–224.

10. Gambichler T, Othlinghaus N, Tomi NS, Holland-Letz T, Boms S, Skrygan M, et al. Medium-dose ultraviolet (UV) A1 vs. narrowband UVB phototherapy in atopic eczema: a randomized crossover study. *Br J Dermatol* 2009; 160: 652–658.
11. Majoie IM, Oldhoff JM, van Weelden H, Laaper-Ertmann M, Bousema MT, Sigurdsson V, et al. Narrowband ultraviolet B and medium-dose ultraviolet A1 are equally effective in the treatment of moderate to severe atopic dermatitis. *J Am Acad Dermatol* 2009; 60: 77–84.
12. Wahlgren CF, Scheynius A, Hägermark O. Antipruritic effect of oral cyclosporin A in atopic dermatitis. *Acta Derm Venereol* 1990; 70: 323–329.
13. Otsuka A, Tanioka M, Nakagawa Y, Honda T, Ikoma A, Miyachi Y, et al. Effects of cyclosporine on pruritus and serum IL-31 levels in patients with atopic dermatitis. *Eur J Dermatol* 2011; 21: 816–817.
14. Nakamura S, Takeda K, Hashimoto Y, Nishi K, Takahashi H, Mizumoto T, et al. Favourable clinical response by pre-prandial administration of low-dose ciclosporin to severe adult atopic dermatitis. *J Dermatolog Treat* 2012; 23: 112–115.
15. Brazzelli V, Prestinari F, Chiesa MG, Borroni RG, Ardigò M, Borroni G. Sequential treatment of severe atopic dermatitis with cyclosporin A and low-dose narrow-band UVB phototherapy. *Dermatology* 2002; 204: 252–254.