Efficacy and safety of medium-dose UVA1 phototherapy in recalcitrant prurigo nodularis: A case report

Nuttaporn Nuntawisuttiwong BSc,
Punyanut Yothachai BSc,
Chutipon Pruksaeakanan MD,
Narumol Silpa-archa MD.

ABSTRACT:

NUNTAWISUTTIWONG N, YOTHACHAI P, PRUKSAEAKANAN C, SILPA-ARCHA N. EFFICACY AND SAFETY OF MEDIUM-DOSE UVA1 PHOTOTHERAPY IN RECALCITRANT PRURIGO NODULARIS: A CASE REPORT. THAI J DERMATOL 2019; 35: 212-217.

DEPARTMENT OF DERMATOLOGY, FACULTY OF MEDICINE, SIRIRAJ HOSPITAL, MAHIDOL UNIVERSITY, BANGKOK, THAILAND.

Prurigo nodularis (PN) is a chronic, pruritic skin condition that is characterized by firm, dome-shaped papules and nodules with varying degrees of central scale, crust, erosion, and ulceration, typically showing a symmetrical distribution. The nodules are intensely pruritic, which leads to the induction of a vicious itch-scratch cycle and reduces quality of life. Although the etiology and pathogenesis remain unclear, cutaneous inflammation and neuronal plasticity seem to play a crucial role in PN[1]. Treatment of PN is challenging because it is usually difficult and requires a multifaceted approach. The most common treatment options include oral antihistamines and topical or systemic corticosteroids. Phototherapy treatment, such as with narrowband ultraviolet B (NB-UVB) and psoralen and ultraviolet A (PUVA), has

From: Department of Dermatology, Faculty of Medicine, Siriraj Hospital Mahidol University, Bangkok, Thailand
Corresponding author: Punyanut Yothachai BSc, email: punyanut_chaaim@hotmail.com

Received: 7 October 2019 Revised: 6 November 2019 Accepted: 7 November 2019

been used as a therapeutic alternative in patients with multiple comorbidities or generalized PN[2]; however, studies on ultraviolet A1 (UVA1) phototherapy are still limited owing to a paucity of randomized controlled trials. We report on a patient with relapsed, severe PN who had undergone a variety of treatments (oral antihistamines; a topical, super-potent corticosteroid; short courses of systemic corticosteroids; and NBUVB phototherapy) and subsequently achieved improvement with UVA1 phototherapy.

Key words: prurigo nodularis; ultraviolet A1; phototherapy

Case Report

A 52-year-old Thai woman, (Fitzpatrick skin type V) with type 2 diabetes mellitus, hypertension, dyslipidemia, and chronic kidney disease stage III presented with numerous, pruritic, excoriated erythematous papules that had been distributed over her trunk and all extremities during the 6 months preceding her visit to our dermatology clinic. She was diagnosed with prurigo nodularis (PN). Because the clinical features were consistent with PN, a skin biopsy was not performed. The therapeutic courses she had been administered for several years beforehand included oral antihistamines; a topical, super-potent corticosteroid; multiple, intermittent, short courses of systemic corticosteroids; and 54 sessions of NB-UVB phototherapy. Although the disease had gradually improved and eventually achieved complete remission, it relapsed 2 years later, displaying a similar extent of nodules and pruritus. She was then treated with a topical super-potent corticosteroid, oral antihistamines, and multiple intralesional injections of corticosteroids; nevertheless, the treatment did not show a good response. She later discontinued the topical corticosteroid, and UVA1 phototherapy was introduced in combination with loratadine 10 mg/day and hydroxyzine 10 mg/day. The patient was treated with medium-dose UVA1 (50 J/cm^2) at a frequency of 3 times per week for 30 sessions. The extent and severity of the disease were assessed by utilizing several tools: The Eczema Area and Severity Index (EASI), a visual analogue scale (with the patient assessing the pruritus severity on a scale between 0 and 10), and the number of lesions. The patient was assessed during the first visit, after every 10 UVA1-phototherapy sessions, at the end of the 30 treatment sessions, and 2 months following the program completion. By 2 months after the therapeutic course, the patient had achieved a decrease in her pruritus and a dramatic improvement in the lesions, without relapse.

Table 1 Results of UVA1 phototherapy and severity assessments for prurigo nodularis in this patient

	First visit	10th treatment	20th treatment	30th treatment	1st month follow-up	2nd month follow-up
Eczema Area and Severity Index	20.2	15.5	13.9	12.9	9.0	10.1
Number of lesions (papules or nodules)	399	375	404	324	382	269
Visual analogue scale	10	5	5	8	5	5
Adverse effects	–	–	–	–	–	–

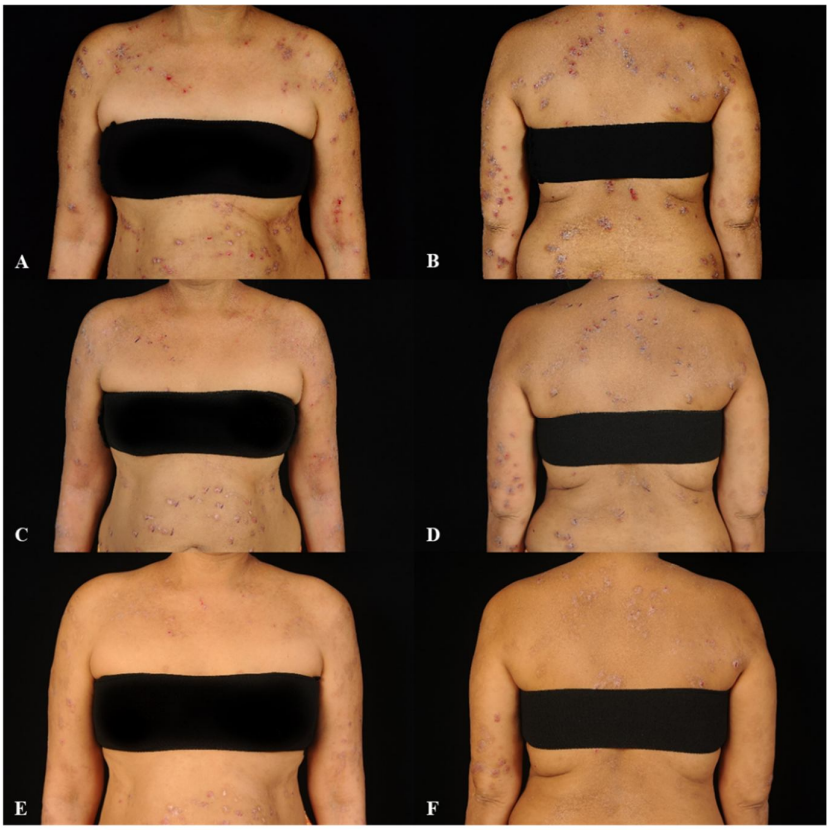

Figure 1 Clinical presentation of the prurigo nodularis before, and at the 10th and 30th treatments of, medium-dosed ultraviolet A1 phototherapy. (A and B, before; C and D, at 10th session; E and F, at 30th session).

Table 2 Reports of PUVA and UVA1 phototherapy for prurigo nodularis

Authors/ year	N	Machine	Mean individual dose (J/cm^2)	Mean no. of irradiations	Mean cumulative dose (J/cm^2)	Outcome measurement	Response	Adverse effects
Divekar et al., 2003[6]	4	Bath PUVA	N/A	N/A	N/A	Clinical response: no response, partial response, and complete response	- 75% of the patients improved - 25% of the patients had complete remission	N/A
	7	Oral PUVA					- 85.7% of the patients improved - 14.3% of the patients had complete remission	N/A
Bruni et al., 2010[10]	23	UVA	N/A	23*	6.07	Physician's clinical evaluation and the patient's subjective assessment$^{\alpha}$	- 78.9% of the patients improved - 52.6% of the patients had complete remission and marked improvement	Mild erythema (2 cases)
Hammes et al., 2011[7]	11	PUVA	N/A	20.4 ± 3.5**	23.7 ± 4.4**	Clinical evaluation: complete remission (> 90%), partial remission (> 50%), and no remission (< 50%)	- All patients improved - 54.5% of the patients had complete remission	Moderate erythema (3 cases)
Rombold et al., 2008[8]	17	UVA1	47.60 ± 9.7**	13.94 ± 6.5**	650.00 ± 379.1**	Grading scale$^{\Psi}$	- 82.4% of the patients showed improvement - 41.1% of the patients had marked improvement	N/A
Present case	1	UVA1	50	30	1,500	- Eczema Area and Severity Index - Number of lesions - Visual analogue scale	Marked improvement in pruritus and moderate improvement in number of lesions	None

*, median number of irradiations; **, data were reported as mean ± standard deviation; $^{\alpha}$, (0) aggravation; (1) no response; (2) slight improvement; (3) marked improvement; (4) complete healing; $^{\Psi}$, (-2) withdrawal after six irradiations; (-1) aggravation; (0) no change; (1) slight improvement; (2) moderate improvement; (3) marked improvement; (4) complete healing

Abbreviations: N/A, not available; PUVA, psoralen and ultraviolet A; UVA1, ultraviolet A1

Table 1 summarizes her clinical response, as assessed by the EASI scores, the number of lesions, and the visual analogue scale scores at each visit. She did not experience any side effects during the course of the UVA1 phototherapy, such as erythema, activation of herpes simplex virus, or induction of polymorphous light eruption.

Discussion

Treatments of PN generally aim to break down the vicious itch-scratch cycle. The current first-line therapies include oral antihistamines, topical corticosteroids, topical calcineurin inhibitors, topical capsaicin, and phototherapy. Systemic treatments (such as low-dose methotrexate, cyclosporine, selective serotonin receptor inhibitors, naltrexone, thalidomide, and lenalidomide) are used in severe cases[3]. Owing to a paucity of data from randomized controlled trials, PN remains difficult to treat, and the therapeutic course often extends over a prolonged period. Phototherapy has been used as a therapeutic alternative in patients with multiple comorbidities or generalized PN[2]. However, there are only a few, small studies available for each of the phototherapy modalities used for the treatment of PN, including PUVA, broadband ultraviolet B (BB-UVB), NB-UVB, excimer laser, and UVA1[4]. Complete remission or dramatic improvements in patients with recalcitrant PN treated with NB-UVB phototherapy alone were reported by Tamagawa-Mineoka et al[5]. PUVA monotherapy has also been reported to be effective for PN[6, 7].

Table 2 demonstrates the efficacy of PUVA and UVA1 for PN. PUVA and UVA1 phototherapies seemed to have no difference in efficacy for the treatment of PN, but patients who were treated with PUVA were more likely to develop erythema than those treated with UVA1 phototherapy. Rombold et al. reported that 14 out of 17 (82.4%) PN patients treated with UVA1 phototherapy alone achieved improvements, with 7 of those patients (41.1%) improving markedly[8]. In our report, the patient also experienced a dramatic improvement in the EASI score and her pruritus. Our study reveals that UVA1 phototherapy alone without a topical corticosteroid can be effective in treating relapsed, severe PN. This seems to be because UVA1 phototherapy has been reported to have an immunomodulatory effect through various mechanisms of action, including induction of T and B lymphocyte apoptosis and suppression of proinflammatory cytokines such as TNF-α and IL-12[9]. UVA1 has a longer wavelength than both UVA and NB-UVB; thus, it can penetrate deeper into the skin; furthermore, it has less ability to produce erythema.

The differences between our case and the Rombold et al.'s study are that our patient has

dark-skinned type compared to Caucasian population and received more sessions of UVA1 phototherapy and a slightly higher single dose than the mean individual dose of the previous study. Even though our patient was treated with more cumulative doses of UVA1 phototherapy than all of those in Rombold et al.'s study, she did not encounter any adverse effects. Both studies demonstrated that medium-dose UVA1 phototherapy can provide substantial improvements to PN, and our study emphasized a good safety profile of UVA1 phototherapy. Still, randomized controlled trials are required to confirm its safety and effectiveness.

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