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**Commentary**

**Phototherapy for the treatment of prurigo nodularis: a review**

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**Abstract**

**Background/Purpose:** Review the available literature on phototherapy for treatment of prurigo nodularis (PN).

**Methods:** Literature search was conducted on MEDLINE.

**Results:** 6 prospective trials, 2 retrospective studies, and 3 case series were found investigating efficacy and safety of phototherapy for treatment of PN.

**Conclusion:** Although large randomized clinical trials are necessary, phototherapy appears to be a safe and efficacious treatment for PN, alone and in combination with other common treatment modalities for PN.

**Introduction**

A debilitating disease characterized by hard, intensely pruritic nodules most commonly on the extensor surfaces of the extremities, prurigo nodularis (PN) was first noted to be responsive to large doses of X-rays in 1924 [1]. Almost a century later, little remains known regarding the etiology and pathophysiology, and given relatively low prevalence, no large randomized-control studies have been done to evaluate the various treatment options used today. Therapies such as superpotent topical corticosteroids, intralesional corticosteroids, topical vitamin D analogs, topical capsaicin, antihistamines, and phototherapy are generally accepted treatment options [2]. Systemic medications such as thalidomide [3], methotrexate [4], and cyclosporine [5] have also been shown to be effective in a small number of studies.

When PN is generalized, the disadvantage to topical therapies is noncompliance given the inconvenience of frequent application to scattered lesions over a large affected body surface area. Systemic agents have various potential internal side effects and the need for frequent laboratory monitoring limit their use. Phototherapy is a treatment option that can be both safe and efficacious, especially for generalized PN. There has been no recent review published regarding PN, and this will be the first comprehensive review focused on phototherapy for the treatment of this condition. The goal is to provide dermatologists with a general update on administering phototherapy to patients with PN. Furthermore, the authors hope to identify any knowledge gaps and serve as direction for future research studies.

**Methods**

Literature search was conducted on MEDLINE using the key phrases “prurigo nodularis” or “nodular prurigo” combined with the phrases “phototherapy” or “ultraviolet therapy”. Literature published between January 1980 and July 2015 in the English language was included for the purpose of this review. Irrelevant articles, review articles, case reports or reports of only 1 subject, and studies that did not report results specific to PN were excluded.

For each article that met the above criteria, the type of study, type of phototherapy modality studied, and number of subjects were identified. When available, dosimetry used in each study was noted, including method for determining starting dose and subsequent dose increments. Treatment course of phototherapy, including mean cumulative dose, mean number of treatments, and mean duration of treatments were also collected. The overall outcome of treatments from each study was summarized, including rates of improvement, relapse, and adverse events.

## Results

Eleven articles met criteria for the purposes of this review, which are listed in Table 1 [6-16]. For each article, the type of study, phototherapy modality utilized, number of subjects, mean cumulative dose, mean number of treatments, and brief summary of the outcomes are recorded. There were 6 prospective trials, 2 retrospective studies, and 3 case series. The most number of studies was on PUVA (bath and/or oral), which totaled 4; PUVA was evaluated alone or in combination with broad-band UVB (BB-UVB) or Excimer laser. There were a total of 3 studies on BB-UVB, alone, in combination with bath PUVA, and as part of a Modified Goeckerman therapy. Two studies evaluated narrow-band UVB (NB-UVB), one alone and another in combination with thalidomide. There were also 2 studies evaluating Excimer laser, one alone and one in combination with superpotent topical steroids. UVA alone was evaluated in 2 studies. The number of subjects in each study varied from as little as 2 in one case series to 63 in one prospective trial (see Table 1).

**Table 1. Summary of the literature reporting use of phototherapy for the treatment of prurigo nodularis**

First author (year)	Type of study	Phototherapy modality	N	Mean cumulative dose (J/cm <sup>2</sup> )	Mean treatment number (range)	Results
Karvonen (1985)	Prospective	PUVA (Trioxsoralen)	63	6.9	14 (6-27)	6% healed, 75% with considerable healing and less pruritus 18% remained in remission at 6 month follow up
Hann (1990)	Case series	BB-UVB + PUVA	2	6.74 + 240	27 (24-30)	Improvement in pruritus and flattening/disappearing of most lesions in both subjects
Ferrándiz (1997)	Prospective	Thalidomide followed by NB-UVB	4	40.5	32 (22-37)	Complete remission in all subjects 1 relapse at 6 month follow up
Divekar (2003)	Retrospective	Bath PUVA Oral PUVA BB-UVB	4 7 8	NA	NA (9-34)	6, 2, and 5 subjects (68%) with partial response with BB-UVB, bath and oral PUVA, respectively 1 subject from each group (15%) with complete response
Tamagawa-Mineoka (2007)	Prospective	NB-UVB	10	23.88	24.3 (10-73)	All subjects with marked/complete improvement 1 relapsed at 1 year follow up
Rombold (2008)	Retrospective	UVA	17	650	13.94 (NA)	82.4% with improvement, 41.1% of which had marked improvement
Saraceno(2008)	Prospective	Excimer	11	13.5	7.45 (6–10)	67% complete remission, 33% partial remission 1 relapsed at 4 month follow up
Hammes (2011)	Randomized prospective	Bath PUVA alone Bath PUVA + Excimer	11 11	23.7 16.9 + 9.0	20.4 (NA) 9.8 (NA)	All subjects in both groups with complete/partial remission Less number of tx's and Lower cumulative dose in combination

						group*
Bruni (2010)	Prospective	UVA	19	6.07	23** (7-37)	78.9% of the subjects with improvement (slight, marked, or complete)
Sorenson (2014)	Case series	Modified Goeckerman (BB-UVB, coal tar, topical steroid)	4	11.8	45.5 (NA)	All subjects with improvement in pruritus and flattening of most lesions 2 subjects relapsed after 2.5 months and 8 months
Nakashima (2014)	Case series	Excimer + potent topical steroid	2	NA	NA	Improvement in pruritus and disappearance of several lesions
*P<0.05, **Median, not mean dose						
BB-UVB: Broad band UVB; NB-UVB: Narrow band UVB; PUVA: Psoralen + UVA; NA: Not available						

With regards to dosimetry, starting dose of phototherapy was determined by formal minimal erythema dose (MED) testing, by MED estimated per patient's skin type, or was not specified. Subsequent dose increments were not specified in most of the studies. Cumulative dose varied depending on type of phototherapy used; specific cumulative dose for each study is listed in Table 1. When looking at dosing frequency, PUVA was administered three times per week in one study, four times per week in another, and unspecified in other studies. Frequency of treatments for UVB was three times per week in two studies, five times per week in another using a modified Goeckerman regimen, and unspecified in remaining studies. For Excimer laser, the studies reported once every other week, once weekly, or twice weekly treatment regimens. Frequency of treatments for UVA phototherapy was not specified in any study. Number of treatment sessions per subject was only available in some studies and varied from as few as 6 total sessions for Excimer laser to as many as 73 in NB-UVB. The mean number of treatment sessions per study varied from 7.45 to 45.5.

Six of the 11 studies showed complete or partial remission in all subjects. The rest of the studies showed at least some improvement in the majority of subjects (see table 1 for specific outcomes). Relapse rates were specified in 3 studies: 1 out of 10 subjects on NB-UVB relapsed at 1 year, 1 out of 4 subjects on NB-UVB following thalidomide therapy relapsed at 6 months, and 2 out of 4 subjects on BB-UVB as part of a Modified Goeckerman therapy relapsed at 2.5 and 8 months. In all studies, adverse outcomes were limited to erythema and increased pruritus; no other adverse events related to phototherapy were reported.

## Discussion

It is well known that PN can be frustrating for both the patient and dermatologist due to difficulty achieving and maintaining satisfactory treatment outcomes. Phototherapy is thought to work in the treatment of PN by decreasing the number of epidermal and dermal nerve fibers related to the calcitonin gene-related peptide (CGRP), which contribute to chronic itch [17]. CGRP and nerve growth factor (NGF) are associated with neural hyperplasia and neurogenic inflammation, which may explain the underlying pathophysiology of PN [18].

On reviewing the literature, there are only a few small studies available on each of the phototherapy modalities used for the treatment of PN, including PUVA, BB-UVB, NB-UVB, Excimer laser, and UVA. All studies show that phototherapy is overall effective in the majority of patients with PN yielding partial, if not complete improvement in appearance of lesions and symptoms of pruritus. There is no clear evidence that one phototherapy modality is superior to another, as none of these had active comparators. Because UVA penetrates deep into the skin, it may be assumed that UVA is more efficacious than UVB in treating PN; however, according to the limited data available so far, UVB and UVA appear to have similar clinical outcomes [9]. Excimer laser does have an additional benefit given its ability to focus on specific resistant nodules. Importantly, various combination therapies including BB-UVB and PUVA, bath PUVA and Excimer, Excimer and potent topical steroid, and Goeckerman therapy (BB-UVB, coal tar, and topical steroid) appear safe and effective. Alone and in combination therapies, the only reported adverse events are erythema and pruritus.

Among the studies reviewed, there was no uniformity with regard to starting dose, dose increments, frequency, and duration of treatment. This is likely because phototherapy is generally started carefully at a low dose and titrated up depending on clinical judgement. Furthermore, each patient's regimen is individualized to maximize safety and efficacy. In theory, guidelines for the starting dosimetry for common conditions such as psoriasis and atopic dermatitis can be used for any other disease provided that the patient does not have a history of photosensitizing disorders or is on a photosensitizing medication. In order to determine

starting dose, formal MED testing, or more conveniently, a dosing protocol by skin type can be used. Both protocols have been shown to be safe given they are conservative estimates, and they also allow for slow dosing increments as tolerated.

Generalized PN is extremely difficult to treat and likely requires more than one treatment modality; the studies reviewed suggest that phototherapy can be an important part of combination therapy. In addition to the combination therapies mentioned above, phototherapy can be used to treat the entirety of involved areas followed by spot-treatment of stubborn lesions with superpotent topical or intralesional corticosteroids. Excimer laser can also be used as a focused treatment modality. Given difficulty in applying topical therapies to all involved body surfaces, this combination approach using phototherapy as generalized therapy may encourage patient compliance.

The limitations to phototherapy include patient availability. While patients may be hesitant to present to the office multiple times per week for phototherapy, a discussion of the alternative methods such as topical therapies (which require application to the entire affected area once or twice per day) and systemic medications (which have potential risks of internal side effects) may guide patients in choosing the best individualized treatment option. Home phototherapy is also possible for some patients. Aside from such logistical barriers, this review indicates that phototherapy is safe with minimal side effects.

Phototherapy is a mainstay treatment modality for many dermatologic conditions including psoriasis and atopic dermatitis. While phototherapy appears to be both safe and effective for the treatment of PN, large randomized clinical trials conducted with uniform outcomes measures are needed. A better understanding of effective frequency, duration, and maintenance regimen to prevent relapse is necessary.

## References

1. Barber HW. Case of prurigo nodularis. *Proc R Soc Med.* 1924;17:3-5.
2. Lee MR, Shumach S. Prurigo nodularis: a review. *Australas J Dermatol.* 2005;46(4):211-8.
3. Alfadley A, Al-Hawsawi K, Thestrup-Pedersen K, Al-Aboud K. Treatment of prurigo nodularis with thalidomide: a case report and review of the literature. *Int J Dermatol.* 2003;42(5):372-5.
4. Spring P, Gschwind I, Gilliet M. Prurigo nodularis: retrospective study of 13 cases managed with methotrexate. *Clin Exp Dermatol.* 2014;39(4):468-73.
5. Berth-Jones J, Smith SG, Graham-Brown RAC. Nodular prurigo responds to cyclosporine. *Br J Dermatol.* 1995;132:795-9.
6. Tamagawa-Mineoka R, Katoh N, Ueda E, Kishimoto S. Narrow-band ultraviolet B phototherapy in patients with recalcitrant nodular prurigo. *J Dermatol.* 2007;34(10):691-5.
7. Ferrándiz C, Carrascosa JM, Just M, Bielsa I, Ribera M. Sequential combination therapy with thalidomide and narrow-band (TL01) UVB in the treatment of prurigo nodularis. *Dermatology.* 1997;195(4):359-61.
8. Sorenson E, Levin E, Koo J, Berger TG. Successful use of a modified Goeckerman regimen in the treatment of generalized prurigo nodularis. *J Am Acad Dermatol.* 2015;72(1):40-2.
9. Divekar PM, Palmer RA, Keefe M. Phototherapy in nodular prurigo. *Clin Exp Dermatol.* 2003;28(1):99-100.
10. Saraceno R, Nisticò SP, Capriotti E, de Felice C, Rhodes LE, Chimenti S. Monochromatic excimer light (308 nm) in the treatment of prurigo nodularis. *Photodermatol Photoimmunol Photomed.* 2008;24(1):43-5.
11. Nakashima C, Tanizaki H, Otsuka A, Miyachi Y, Kabashima K. Intractable prurigo nodularis successfully treated with combination therapy with a newly developed excimer laser and topical steroids. *Dermatol Online J.* 2014;20(6) pii: 13030/qt9xp4640d.
12. Hammes S, Hermann J, Roos S, Ockenfels HM. UVB 308-nm excimer light and bath PUVA: combination therapy is very effective in the treatment of prurigo nodularis. *J Eur Acad Dermatol Venerol.* 2011;25(7):799-803.
13. Hann SK, Cho MY, Park YK. UV treatment of generalized prurigo nodularis. *Int J Dermatol.* 1990;29(5):436-7.
14. Karvonen J, Hannuksela M. Long term results of topical trioxsalen PUVA in lichen planus and nodular prurigo. *Acta Dermatovener.* 1985;120:53-5.
15. Bruni E, Caccialanza M, Piccinno R. Phototherapy of generalized prurigo nodularis. *Clin Exp Dermatol.* 2010;35(5):549-50.
16. Rombold S, Lobisch K, Katzer K, Graziotin TC, Ring J, Eberlein B. Efficacy of UVA1 phototherapy in 230 patients with various skin diseases. *Photodermatol Photoimmunol Photomed.* 2008;24(1):19-23.
17. Wallengren J, Sundler F. Phototherapy reduces the number of epidermal and CGRP-positive dermal nerve fibres. *Acta Derm Venereol.* 2004;84(2):111-5.
18. Liang Y, Jacobi HH, Reimert CM, et al. CGRP-immunoreactive nerves in prurigo nodularis: an exploration of neurogenic inflammation. *J Cutan Pathol.* 2000;27(7):359-66.