**Systematic Review of Phototherapy in Pruritic Disorders**

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Abstract

Phototherapy is a proven method for the management of many pruritic disorders, including atopic dermatitis (AD), prurigo nodularis (PN), and generalized pruritus (GP). Objective: This review aims to give an update on the use of phototherapy for managing pruritus in these disorders to establish it within the spectrum of possible therapeutic options. Methods: A thorough literature search of the PubMed database was conducted to identify studies that examined a variety of phototherapy methods in these disorders. Results: AD is best managed with narrow band (NB)-UVB. NB-UVB and broad band (BB)-UVB are also effective in decreasing pruritus in PN. BB-UVB is the preferred modality to decrease GP caused by uric pruritus (UP). Conclusion: Phototherapy is a safe and beneficial option when other measures fail to control pruritus in these disorders.

Introduction

Pruritus, or the sensation of itch, is the most common symptom among dermatology patients. Both cutaneous and systemic conditions may present with pruritus as the primary symptom. Chronic pruritus is a major cause of distress to patients and has a significant impact on quality of life. All ages are affected by pruritus, ranging from children to seniors, and it is the most common dermatologic complaint in the latter group. For many sufferers of pruritus, topical therapy is not adequate in controlling their symptom. Therefore, providing additional therapeutic options becomes essential for the successful dermatologist. Phototherapy is a safe and efficacious management modality that decreases pruritus and can be used across age groups.

Ultraviolet-based therapy (phototherapy and photochemotherapy) can provide relief for pruritic patients without many of the risks and adverse effects of systemic medications. UVB (290-320 nm) and UVA (320-400 nm) are implemented in UV-based therapy. Broadband UVB (BB-UVB) and broadband UVA (BB-UVA) use a light source covering their entire spectrum. Narrowband UVB (NB-UVB) uses 311-313 nm, and UVA1 uses 340-400 nm with a peak at 365 nm. UVUVA1 can be administered at high-dose (HD-UVA1) (130 J/cm²), medium-dose (MD-UVA1) (50 J/cm²), and low-dose (LD-UVA1) (20 J/cm²). Monochromatic excimer light (308 nm), or MEL, is a more targeted phototherapy device that delivers 308 nm UVB to a localized area and can expand treatment options by sparing unaffected areas. This review article focuses on the efficacy of these forms of phototherapy to treat non-psorias, chronic, pruritic disorders triggered by an inflammatory response including atopic dermatitis (AD), prurigo nodularis (PN), lichen simplex chronicus (LSC), and generalized pruritus (GP). To our knowledge, this type of review has not been published before for phototherapy of pruritus.

Methods

For this systematic review, we concentrated on the therapeutic role of phototherapy for AD, PN, LSC, and GP in adults. The computerized bibliographic database PubMed was used to conduct a search for English articles from inception to August 2014. Research articles of randomized controlled trials (RCT), open prospective studies, pilot studies, and retrospective observations on NB-UVB, BB-UVB, UVA, PUVA, and MEL were used. The following key words were used: phototherapy pruritus, phototherapy eczema, phototherapy atopic dermatitis, phototherapy prurigo nodularis, phototherapy lichen simplex chronicus, phototherapy neurodermatitis, and phototherapy pruritic disorders. Based on the keywords chosen, 1,194 articles were revealed. After screening title and abstract, those studies in which phototherapy was not used as a treatment for the chosen disease processes were excluded. Reference lists in review articles were also searched. Abstracts-only and duplicates were excluded. This left 105 articles for the screening phase. These records were then assessed for eligibility, excluding children, hand eczema, nummular eczema, and other modes of treatment as primary analysis, thereby leaving 58 studies. Relevant data including study design, number of participants, duration of treatment, cumulative phototherapy dosing, adverse effects, and clinical outcome were retrieved from the articles and formulated into spreadsheet databases. Thus, the total number of trials included in the final analysis is 58. When specific pruritus assessment scales were mentioned, we cited them in the results. If no particular assessment scale was used, extent of disease, sleep improvement, and remission were evaluated. Because pruritus is the main symptom of these disorders, the above criteria may be considered synonymous with the resolution of pruritus.

Results

We separated our data based on our disease processes of interest, and further viewed each category of phototherapy based on current widespread availability and use.

Atopic Dermatitis

AD is a common, chronic inflammatory skin disease characterized by intense pruritus leading to secondary cutaneous findings. It is a genotypic diathesis in which a heightened immune response is triggered once the skin is irritated by an environmental stimulus, subsequently producing the sensation of itch. Genetically predisposed individuals have an imbalance in the T-helper (Th) 2 versus Th1 immune responses. AD develops secondary to this intensified immune response once the patient continuously scratches. Hence, AD is colloquially known in dermatology as “the itch that rashes,” because the itch is the chief symptom and the foremost indicator of treatment efficacy.

NB-UVB:

The reduction of pruritus in AD by NB-UVB radiation has been demonstrated in multiple studies (Table 1). A double-blind RCT was conducted by Reynolds et al. to compare the efficacy of NB-UVB to BB-UVA and a placebo of visible fluorescent light. The NB-UVB group experienced a 90% reduction in pruritus from baseline, compared to 63% reduction in the BB-UVA group. When compared to placebo, there was a 38% greater reduction in pruritus for NB-UVB versus an 11% reduction for BB-UVA. Seventy-one percent of patients had an improvement in their loss of sleep when on NB-UVB, as opposed to 53% on BB-UVA. NB-UVB also showed an improvement in disease activity in the three-month follow-up period. Although patients in this study were allowed to use moderate-to-potent topical steroids simultaneously, their use was quantified and included in the evaluation of treatment efficacy. This is in line with the real-world usage of phototherapy, as dermatologists rarely use phototherapy-only in practice. Other studies that evaluated the use of NB-UVB support these positive results. In a nonrandomized, single-blind, half-side comparison study between NB-UVB and the combination treatment of UVA and UVB (UVAB), NB-UVB significantly reduced pruritus (mean visual analogue scores 2.7 and 3.8; p=0.043). Legat et al. conducted...
Table 1: Phototherapy for treatment of pruritus in atopic dermatitis (AD)

<table>
<thead>
<tr>
<th>Study Type</th>
<th>Participants (no.)</th>
<th>Treatment Regimen</th>
<th>Cumulative Dose (J/cm²)</th>
<th>Concomitant TCS allowed</th>
<th>Pruritus Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>NB-UVB</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>RCT, open8</td>
<td>21</td>
<td>3x/wk for 12 wks</td>
<td>NB-UVB: 35.05</td>
<td>Yes</td>
<td>- 68% reduction in AD severity scores - 88% reduction in TCS use</td>
</tr>
<tr>
<td>RCS9</td>
<td>37</td>
<td>2x/wk</td>
<td>NB-UVB: 21.9</td>
<td>Yes</td>
<td>81% improved</td>
</tr>
<tr>
<td>RCS18</td>
<td>40</td>
<td>3x/wk</td>
<td>NB-UVB: 16.371</td>
<td>Yes</td>
<td>80% improved</td>
</tr>
<tr>
<td>RCS, BCS12</td>
<td>10</td>
<td>3x/wk for 6 wks</td>
<td>NB-UVB: NR UVAB: NR</td>
<td>Yes</td>
<td>NB-UVB &gt; UVAB</td>
</tr>
<tr>
<td>RCS, BCS13</td>
<td>9</td>
<td>3x/wk for 8 wks</td>
<td>NB-UVB: 26.7 MD-UV A1: 1000</td>
<td>No</td>
<td>NB-UVB = MD-UV A1</td>
</tr>
<tr>
<td>RCS, BCS14</td>
<td>13</td>
<td>3x/wk for 8 wks</td>
<td>NB-UVB: 10.5 MD-UV A1: 930.6</td>
<td>In follow-up period</td>
<td>NB-UVB = MD-UV A1</td>
</tr>
<tr>
<td>RCS, CoS15</td>
<td>47</td>
<td>3x/wk for 6 wks</td>
<td>NB-UVB: 23.4 MD-UV A1: 880</td>
<td>No</td>
<td>NB-UVB = MD-UV A1</td>
</tr>
<tr>
<td>RCT11</td>
<td>5</td>
<td>5x/wk for 3 wks</td>
<td>NB-UVB: 9.2</td>
<td>No</td>
<td>100% patients improved</td>
</tr>
<tr>
<td><strong>BB-UVB</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>RCS, BCS16</td>
<td>17</td>
<td>3x/wk for 8 wks</td>
<td>BB-UVB: NR Daylight tubes (placebo): NA</td>
<td>Yes</td>
<td>BB-UVB &gt; placebo</td>
</tr>
<tr>
<td>CS17</td>
<td>1*</td>
<td>2x/wk for 3 months</td>
<td>BB-UVB: NR</td>
<td>No</td>
<td>BB-UVB &gt; NB-UVB</td>
</tr>
<tr>
<td>RCT19</td>
<td>BB-UVB: 52 UVAB: 54</td>
<td>5x/wk</td>
<td>BB-UVB: 2.70 UVAB: 1.77 (UVB), 104 (5)</td>
<td>No</td>
<td>UVAB &gt; BB-UVB</td>
</tr>
<tr>
<td>RCT20</td>
<td>89</td>
<td></td>
<td></td>
<td></td>
<td>UVAB &gt; BB-UVB</td>
</tr>
<tr>
<td>RCT21</td>
<td>BB-UVB: 33 UVAB: 23</td>
<td>5x/wk</td>
<td>BB-UVB: 2.3 UVAB: 1.4 (UVB) 160 (5)</td>
<td>Yes</td>
<td>UVAB &gt; BB-UVB</td>
</tr>
<tr>
<td><strong>PUVA</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>RCS, BCS23</td>
<td>- Whole-body PUVA vs. control: 5 - PUVA vs. no treatment: 5 - PUVA vs. BB-UVB: 5</td>
<td>PUVA: 3x/wk BB-UVB: 5x/wk</td>
<td>PUVA: 13 - No treatment: NR BB-UVB: NR</td>
<td>No</td>
<td>PUVA &gt; BB-UVB &amp; placebo</td>
</tr>
<tr>
<td>RCT24</td>
<td>113</td>
<td>PUVA: 3x/wk for 8 wks</td>
<td>PUVA: 115.3</td>
<td>80% decrease in severity</td>
<td></td>
</tr>
<tr>
<td>RCT, BCS27</td>
<td>12</td>
<td>PUVA: 3x/wk for 6 wks</td>
<td>BB-UVB: 14 Bath PUVA: 48.3</td>
<td>No</td>
<td>PUVA = NB-UVB</td>
</tr>
<tr>
<td>CoS2</td>
<td>40</td>
<td>MOP+UV A: 3x/wk for 5 wks MD-UV A1: 5x/wk for 3 wks</td>
<td>PUVA: 48.1 MD-UV A1: 1138.8</td>
<td>No</td>
<td>PUVA &gt; MD-UV A1</td>
</tr>
<tr>
<td><strong>UVA1</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>RCS, BCS29</td>
<td>- UVA + UVAB: 28 BB-UVB + UVAB: 20</td>
<td>UVA + UVAB: 5x/wk for 3 wks BB-UVB + UVAB: 3x/wk for 8 wks</td>
<td>UVA (361) + UVAB: 0.466 (UVB), 109 (5) BB-UVB (0.282) + UVAB: 0.558 (UVB) 130 (5)</td>
<td>Yes</td>
<td>- UVA = UVAB UVAB &gt; BB-UVB</td>
</tr>
</tbody>
</table>
a randomized, nonblinded comparison of NB-UVB to MD-UVA1 and found them equally efficacious in reducing pruritus, a claim supported by other, similar studies.\textsuperscript{13-15} Taken together, these trials suggest NB-UVB as a preferred treatment for AD.

\textbf{BB-UVB:}\n
BB-UVB has largely been replaced by NB-UVB in today’s dermatology clinics, as more studies have demonstrated the superior efficacy of NB-UVB in treating psoriasis. However, there is a small subset of eczematous patients who are unable to tolerate NB-UVB but can tolerate BB-UVB. Previous studies have demonstrated the superiority of BB-UVB to placebo in treating AD, with a 76% improvement in patients (p < 0.001).\textsuperscript{16} Pugashetti et al. reported the case of an AD patient in whom NB-UVB caused irritation and was less effective when compared to BB-UVB.\textsuperscript{17} The authors hypothesized that the higher doses required by NB-UVB to achieve minimal erythema and induce apoptosis resulted in burning and cutaneous sensitivity, which was not experienced during BB-UVB treatments.\textsuperscript{17,18} Finally, a few studies found the combination of BB-UVB with UVA superior to BB-UVB alone.\textsuperscript{19-21} However, BB-UVB was comparable to LD-UVA1 in improving the pruritus score.\textsuperscript{22}

\textbf{PUVA:}\n
The use of PUVA in AD treatment dates back to the 1970s, when Morrison et al. demonstrated 8-methoxypsoralen (8-MOP) PUVA as superior to both placebo and BB-UVB.\textsuperscript{21} 8-MOP PUVA has resulted in an 80% decrease in pruritus severity, and 5-MOP PUVA has caused a greater reduction in SCORAD than MD-UVA1 (mean +/- SD 54.3 +/- 25.7% vs. 37.7 +/- 22.8%; p = 0.041).\textsuperscript{24-26} The average length of remission was also longer for PUVA than MD-UVA1 (12 weeks vs. 4 weeks; p = 0.012). Bath PUVA was compared with both NB-UVB in an investigator-blinded half-side study.\textsuperscript{27} It yielded no significant difference when evaluated using SCORAD (65.7% vs. 64.1%; p = 0.48), even though a faster response to bath PUVA was noted during the first two weeks.

\textbf{UVA:}\n
Older studies have compared the traditional combination UVA and BB-UVB (UVAB) to UVA1 and other types of phototherapy. UVA1 was found to be superior to BB-UVB in decreasing pruritus.\textsuperscript{28} Another study by the same group compared two groups receiving either UVA + UVAB or BB-UVB + UVA1, without a control group.\textsuperscript{29} There was an equal improvement in pruritus when comparing UVA to UVA1, but a significant difference in favor of UVA1 when comparing BB-UVB to UVA1. When assessed by the Costa overall score, HD-UVA1 proved to be more effective than UVA1 in decreasing the severity of itch symptoms (50% after six treatments vs. 30% after 15 treatments).\textsuperscript{30} This suggested a fast-acting therapeutic action for HD-UVA1 and a slow-acting mechanism for UVAB. This was further examined in a study randomizing patients into groups of HD-UVA1, UVAB, or mid-potency corticosteroids. HD-UVA1 was the most effective for decreasing pruritus in acute, severe exacerbations of AD patient in whom NB-UVB caused irritation, and was less effective when compared to BB-UVB. The authors hypothesized that the higher doses required by NB-UVB to achieve minimal erythema and induce apoptosis resulted in burning and cutaneous sensitivity, which was not experienced during BB-UVB treatments. Finally, a few studies found the combination of BB-UVB with UVA superior to BB-UVB alone. However, BB-UVB was comparable to LD-UVA1 in improving the pruritus score.

UVAB was found to be superior to BB-UVB in decreasing pruritus.\textsuperscript{28} Another study by the same group compared two groups receiving either UVA + UVAB or BB-UVB + UVA1, without a control group.\textsuperscript{29} There was an equal improvement in pruritus when comparing UVA to UVA1, but a significant difference in favor of UVA1 when comparing BB-UVB to UVA1. When assessed by the Costa overall score, HD-UVA1 proved to be more effective than UVA1 in decreasing the severity of itch symptoms (50% after six treatments vs. 30% after 15 treatments).\textsuperscript{30} This suggested a fast-acting therapeutic action for HD-UVA1 and a slow-acting mechanism for UVAB. This was further examined in a study randomizing patients into groups of HD-UVA1, UVAB, or mid-potency corticosteroids. HD-UVA1 was the most effective for decreasing pruritus in acute, severe exacerbations of AD.

\begin{table}[h]
\centering
\begin{tabular}{|c|c|c|c|c|}
\hline
RCT, BCS\textsuperscript{*} & 10 & 5x/wk for 3 wks & - HD-UVA1: 1710 & No & HD-UVA1 = MD-UVA1 \\
\hline
RCT\textsuperscript{**} & MD-UVA1: LD-UVA1: & 5x/wk for 3 wks & - MD-UVA1: 50 & No & MD-UVA1 > LD-UVA1 \\
\hline
RCT\textsuperscript{**} & 32 & 5x/wk for 3 wks & MD-UVA1: 750 & No & SCORAD improved by 34%; 10% deterioration after 1 month; 40% deterioration after 3 months \\
\hline
\end{tabular}
\caption{UVAB}
\end{table}

\begin{table}[h]
\centering
\begin{tabular}{|c|c|c|c|c|}
\hline
RCT, BCS\textsuperscript{**} & 39 & 3x/wk for 8 wks & - UVAB: NR & Yes & UVAB > BB-UVB \\
\hline
\end{tabular}
\caption{RCT, BCS}
\end{table}

*The other cases in this case series were excluded because they did not pertain to AD

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UVAB has also been reported to be beneficial in the treatment of PN.\textsuperscript{39,43,45} A complete response or significant improvement was found in most patients treated with bath PUVA.\textsuperscript{52,53} There was a greater reduction in papules, infiltration of T cells, and pruritus (PIP) score in patients treated with bath PUVA and MD UVA1 compared to those treated with NB-UVB (P<0.01, 95% CI 1.1-3.36 and P<0.05, 95% CI 0.42-2.70, respectively).\textsuperscript{45} On a six-week follow-up, however, all patients relapsed except for 30% of those treated with NB-UVB and 9% of those

\textbf{Prurigo Nodularis:}\n
Prurigo nodularis (PN) is a chronic inflammatory skin condition with nodular pruritic lesions. An intense itch-scratch cycle, similar to that in AD, induces chronic excoriated pruritic nodules that appear most commonly on the extremities, neck, and shoulders. The exact etiology and mechanism of PN remain elusive; however, it has been associated with atopy, pregnancy, HIV, psychiatric disorders, internal diseases, and malignancy.\textsuperscript{36-39} The mechanisms for these associations are unclear as they are mainly derived from case reports. The primary goal of treatment is to decrease pruritus, which can be achieved via topical and intralesional corticosteroids, tacrolimus, calcipotriol, cryotherapy, capsaicin, thalidomide, cyclosporine, or phototherapy.\textsuperscript{39,41} UV-light exposure diminishes pruritus in PN due to its anti-inflammatory effects, in a manner similar to that seen in AD.\textsuperscript{42,43}

\textbf{NB-UVB:}\n
NB-UVB has not only resulted in the improvement of lesions but has also provided for long-term remission upon one-year follow-up.\textsuperscript{44} Combining NB-UVB with thalidomide has also provided excellent results in the treatment of PN and is considered by some as the treatment of choice for PN.\textsuperscript{40,46} However, there is concern for its teratogenic effects and potential for inducing dose-related peripheral neuropathy.\textsuperscript{46,47} Thus, reducing total treatment time and dosage of thalidomide by combining it with NB-UVB is a better therapeutic option.\textsuperscript{40}

\textbf{BB-UVB:}\n
While NB-UVB is thought to be more efficacious in the treatment of PN, BB-UVB has also proved beneficial.\textsuperscript{39,45,48} A study in England found seven out of eight patients cleared of PN and with decreased pruritus with the use of BB-UVB.\textsuperscript{49} Combination treatment of UVB with topical PUVA provided successful results.\textsuperscript{50}
Table 2: Phototherapy for treatment of pruritus in prurigo nodularis (PN)

<table>
<thead>
<tr>
<th>Study Type</th>
<th>Participants (no.)</th>
<th>Treatment Regimen</th>
<th>Cumulative Dose (J/cm²)</th>
<th>Concomitant TCS allowed</th>
<th>Pruritus Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>NB-UVB</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PCS44</td>
<td>10</td>
<td>NB-UVB: 1x/week for mean 24.3 irradiations</td>
<td>NB-UVB: 23.88</td>
<td>No</td>
<td>Improved, with long remission</td>
</tr>
<tr>
<td>RCT46</td>
<td>4</td>
<td>- NB-UVB: 3x/wk for 32 irradiations - Thalidomide therapy: 100mg/day for 12 wks</td>
<td>- NB-UVB: 40.5 - Thalidomide therapy: NA</td>
<td>NR</td>
<td>Excellent response to thalidomide after 8-10 wks; well-controlled with NB-UVB</td>
</tr>
<tr>
<td><strong>BB-UVB</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CR59</td>
<td>8</td>
<td>BB-UVB: NR</td>
<td>BB-UVB: NR</td>
<td>NR</td>
<td>50% improved</td>
</tr>
<tr>
<td>CS59</td>
<td>- BB-UVB: 8 - Bath PUVA: 4 - Oral PUVA: 7</td>
<td>19 courses of phototherapy</td>
<td>- BB-UVB: NR - Bath PUVA: 7.5 mL 1.2% 8-MOP bath solution diluted in 70L of water - Oral PUVA: 8-MOP, 25 mg/m²</td>
<td>NR</td>
<td>- BB-UVB: 87.5% partial/complete resolution - Bath PUVA: 75% partial/complete resolution - Oral PUVA: 85.7% partial/complete resolution</td>
</tr>
<tr>
<td>CS59</td>
<td>Case 1</td>
<td>- BB-UVB: 3x/wk for 6 wks - 8-MOP Topical PUVA: 3x/wk for 8 wks</td>
<td>- BB-UVB: 6234 - 8-MOP Topical PUVA: 240</td>
<td>Yes</td>
<td>Well-controlled lesions and itch</td>
</tr>
<tr>
<td></td>
<td>Case 2</td>
<td>30 irradiations</td>
<td>- BB-UVB: 7239 - 8-MOP Topical PUVA: 240</td>
<td>NR</td>
<td>Well-controlled lesions and itch</td>
</tr>
<tr>
<td><strong>PUVA</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>RCT50</td>
<td>63</td>
<td>14 irradiations</td>
<td>PUVA: 6.9</td>
<td>NR</td>
<td>81% improved</td>
</tr>
<tr>
<td>RCT50</td>
<td>17</td>
<td>8 wks</td>
<td>PUVA: 30.3</td>
<td>NR</td>
<td>88% significantly improved, sustained improvement on 6-wk follow-up</td>
</tr>
<tr>
<td>RCT50</td>
<td>10</td>
<td>Until clinical improvement or minor erythema</td>
<td>PUVA: 19</td>
<td>NR</td>
<td>Median of 13 baths for clearing of pruritic lesions</td>
</tr>
<tr>
<td>RCT54</td>
<td>15</td>
<td>Until beneficial results</td>
<td>PUVA: 14.6</td>
<td>NR</td>
<td>53% showed good result by average 3 wks</td>
</tr>
<tr>
<td><strong>MEL</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PS56</td>
<td>11</td>
<td>once/wk for 8 wks</td>
<td>MEL: 13.5</td>
<td>No</td>
<td>81% had partial or complete remission</td>
</tr>
<tr>
<td>RCT57</td>
<td>22</td>
<td>- PUVA + MEL: 2x/wk for 5 wks - PUVA: 4x/wk for 5 wks</td>
<td>- PUVA + MEL: 23.7 - PUVA: 16.9</td>
<td>NR</td>
<td>Average of 5 fewer PUVA treatments in combination group; 100% remission in PUVA group; 90% remission in combination group</td>
</tr>
<tr>
<td><strong>UVA</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>RCS52</td>
<td>17</td>
<td>13.94 mean irradiations</td>
<td>650</td>
<td>NR</td>
<td>82.4% improved</td>
</tr>
<tr>
<td>RCS55</td>
<td>19</td>
<td>23 median treatments</td>
<td>6.07</td>
<td>No</td>
<td>78.9% improved</td>
</tr>
</tbody>
</table>

BCS: bilateral comparison study; CR: case report; CS: case series; CoS: crossover study; NA: not applicable; NR: not reported; PCS: prospective cohort study; PS: pilot study; RCT: randomized controlled trial; RCS: retrospective cohort study; TCS: topical corticosteroid

treated with MD UVA1. While this seems to indicate that PUVA loses its effect quickly, 86% of patients in another study extended into the maintenance phase.54

**MEL:**
MEL has also been used to target the pruritic nodules.55,56 Nistico et al. observed a decrease in pruritic symptoms in all nine PN patients they studied. MEL provides a more targeted approach and reduces the total number of treatments needed to reach remission. A combination study comparing PUVA + MEL to PUVA alone demonstrated the decreased need for overall treatments in the combination group, although both groups were successful in improving eruptions and achieving complete clearance.57 Long-term benefits of reduced itching were also noted.

**UVA:**
There are a limited number of studies on the efficacy of UVA1 for PN treatment, with 82.4% improvement in pruritus in one study and 78.9% in another.42,58 The latter group used a UVA lamp with a spike at 390 nm for deeper penetration as the biological effects of UV radiation are directly proportional to its wavelength. Bath PUVA and MD UVA1 have longer wavelengths and therefore are more capable of penetrating the thickened epidermis of PN.39,59
Lichen Simplex Chronicus

LSC, also termed neurodermatitis, is a secondary skin disorder that results from excessive scratching. Thus, therapeutic options depend on interrupting the itch-scratch cycle. LSC is often associated with an atopic disorder and is similar to PN in pathogenesis. Lichenification results from thickening of epidermis (acanthosis) and stratum corneum (hyperkeratosis) from the constant trauma of rubbing and scratching for roughly 90 hours, or 140,000 scratches. A case of vulvar LSC was treated with NB-UVB light source, signifying the tolerability of NB-UVB even in sensitive areas. Similar to MEL, a 311-nm comb light device was used thrice a week. Pruritus was assessed by a visual analogue scale with increased intracorneal cohesion and no difference in response to intradermal histamine. Xerosis was found to be proportional to the degree of itch, and vascular response to histamine. Xerosis decreases, along with sweat and sebum production and vascular response to histamine. Xerosis was found to be proportional to the degree of itch, and vascular response to histamine.

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Generalized Pruritus

GP is chronic itch that occurs without any associated diagnosable skin diseases or primary skin lesions. Although frequently idiopathic, it can be secondary to neurologic disorders, chronic renal failure, cholestasis, systemic infections, malignancies, and endocrine disorders. A judicious history, thorough physical examination, and suitable laboratory investigation must be performed to elucidate the cause. Systemic disease has been implicated in up to 20% of patients with GP. Special emphasis should be placed on drug exposure, travel history, environmental irritants, lifestyle, extracutaneous symptoms, and prior hospitalizations. Initial laboratory tests may include complete blood count, liver- and renal-function tests, serum glucose, iron, ferritin, thyroid-function tests, erythrocyte sedimentation rate, protein electrophoresis, and urinalysis. Many cases of GP begin in a localized area, and phototherapy can often lead to cessation of generalized itch and reveal a previously localized itch. Generalization can be caused by a lowering of itch threshold on other body parts through a combination of neurologic and/or psychological mechanisms.

Those with a negative workup for GP fall into idiopathic pruritus (IP). In those over the age of 65, this form of idiopathic itch is often dubbed "senile pruritus" or Willan's itch, as it is often associated with dry skin. The stratum corneum thickens with age and has decreased keratohyalin granules. Elderly patients with dry skin have a decreased number of surface lipids, impairing the stratum corneum's ability to hold water. Clearance of debris from the dermis also impairs the stratum corneum's ability to hold water. These changes can lead to decreased barrier function, increased transepidermal water loss, and increased pruritus.

### Table 3: Phototherapy for treatment of pruritus in uremic pruritus (UP)

<table>
<thead>
<tr>
<th>Study Type</th>
<th>Participants (no.)</th>
<th>Treatment Regimen</th>
<th>Cumulative Dose (J/cm²)</th>
<th>Pruritus Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>RCS⁷⁷</td>
<td>6</td>
<td>33 irradiations</td>
<td>NB-UVB: 52</td>
<td>33% had significant improvement (66-100% resolution of lesions and/or reduction of pruritus intensity)</td>
</tr>
<tr>
<td>RCT⁸⁸</td>
<td>- UP: 22 - IP: 22</td>
<td>3x/wk for 22 irradiations</td>
<td>NB-UVB - for UP: 24.54 - NB-UVB for IP: 20.801</td>
<td>- UP: 60% had &gt;50% improvement - IP: 68% had &gt;50% improvement</td>
</tr>
<tr>
<td>RCT⁹⁹</td>
<td>10</td>
<td>3x/wk for 6 wks</td>
<td>NB-UVB: NR</td>
<td>70.8% decrease with 43% in remission after 6 months</td>
</tr>
<tr>
<td>RCT¹⁰¹</td>
<td>21</td>
<td>3x/wk for 6 wks</td>
<td>NB-UVB: NR - UVA: 1-6</td>
<td>NB-UVB = UVA</td>
</tr>
<tr>
<td>RCT¹⁰²</td>
<td>18</td>
<td>2x/wk for 4 wks</td>
<td>BB-UVB: NR</td>
<td>90% had decreased pruritus</td>
</tr>
<tr>
<td>RCS¹⁰⁴</td>
<td>- BB-UVB: 9 - UVA: 8</td>
<td>3x/wk for 2 wks</td>
<td>BB-UVB: NR</td>
<td>BB-UVB &gt; UVA</td>
</tr>
<tr>
<td>CoS⁸⁵</td>
<td>20</td>
<td>2x/wk for 4 wks</td>
<td>BB-UVB: NR</td>
<td>BB-UVB = UVA</td>
</tr>
<tr>
<td>RCT¹⁰⁶</td>
<td>10</td>
<td>12 irradiations</td>
<td>BB-UVB: 7.9 - UVA: 1.3</td>
<td>70% had relief</td>
</tr>
<tr>
<td>RCT¹⁰⁸</td>
<td>10</td>
<td>2x-3x/wk</td>
<td>BB-UVB: NR</td>
<td>80% had complete relief</td>
</tr>
<tr>
<td>RCT¹⁰⁹</td>
<td>14</td>
<td>NR</td>
<td>BB-UVB: NR</td>
<td>57% had objective benefit, 100% had decreased itch intensity</td>
</tr>
<tr>
<td>CR¹⁰⁹</td>
<td>1</td>
<td>- BB-UVB: a) 1st course: 8 irradiations b) 2nd course: 10 Irradiations c) 3rd course: 6 Irradiations</td>
<td>- 1st course: 0.12 - 2nd course: 0.23 - 3rd course: 0.76 - NB-UVB: 2</td>
<td>BB-UVB &gt; NB-UVB</td>
</tr>
</tbody>
</table>

**NB-UVB** is not statistically significant; **BB-UVB** is significantly different from NB-UVB. 

**BCS**: bilateral comparison study; **CR**: case report; **CS**: case series; **CoS**: crossover study; **NA**: not applicable; **NR**: not reported; **PCS**: prospective cohort study; **PS**: pilot study; **RCT**: randomized controlled trial; **RCS**: retrospective cohort study; **TCS**: topical corticosteroid; **UP**: uremic pruritus; **IP**: idiopathic pruritus

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**NB-UVB** and **BB-UVB** are key light sources for phototherapy in uremic pruritus (UP). Table 3 highlights the cumulative doses and pruritus outcomes of various phototherapy regimens, including the use ofBB-UVB and UV A. This table is crucial for understanding the efficacy of different phototherapy treatments in managing uremic pruritus, a distressing disease with no clear pathophysiology. The data suggests that phototherapy, particularly with BB-UVB, can lead to significant improvement and resolution of pruritus, with outcomes varying among different study populations and treatment regimens.

### Lichen Simplex Chronicus

LSC, also termed neurodermatitis, is a secondary skin disorder that results from excessive scratching. Thus, therapeutic options depend on interrupting the itch-scratch cycle. LSC is often associated with an atopic disorder and is similar to PN in pathogenesis. Lichenification results from thickening of epidermis (acanthosis) and stratum corneum (hyperkeratosis) from the constant trauma of rubbing and scratching for roughly 90 hours, or 140,000 scratches. A case of vulvar LSC was treated with NB-UVB light source, signifying the tolerability of NB-UVB even in sensitive areas. Similar to MEL, a 311-nm comb light device was used thrice a week. Pruritus was assessed by a visual analogue scale with increased intracorneal cohesion and no difference in response to intradermal histamine. Xerosis was found to be proportional to the degree of itch, and vascular response to histamine. Xerosis decreases, along with sweat and sebum production and vascular response to histamine. Xerosis was found to be proportional to the degree of itch, and vascular response to histamine. Xerosis decreases, along with sweat and sebum production and vascular response to histamine.

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Those with a negative workup for GP fall into idiopathic pruritus (IP). In those over the age of 65, this form of idiopathic itch is often dubbed "senile pruritus" or Willan's itch, as it is often associated with dry skin. The stratum corneum thickens with age and has decreased keratohyalin granules. Elderly patients with dry skin have a decreased number of surface lipids, impairing the stratum corneum's ability to hold water. Clearance of debris from the dermis also decreases, along with sweat and sebum production and vascular response to histamine. Xerosis was found to be proportional to the degree of itch, with increased intracorneal cohesion and no difference in response to intradermal histamine. Of all the systemic disorders linked to pruritus,
uremia is the most common. Sixty-eight percent of those with chronic renal failure (CRF) and 90% of those receiving dialysis have uremic pruritus (UP). Up to 50% of UP patients complain about generalized pruritus. In the remaining, UP predominantly affects the back, face, and shunt-arm. The term uremic pruritus is not apt because UP does not result from an increase in serum-urea levels. Clinically, UP skin resembles that of hemodialysis patients without pruritus, dry and scaly. No primary skin lesions are seen; however, chronic excoriations, linear crusts, and ulcerations can evolve into a presentation similar to that of PN. Pruritus of hemodialysis and that of peritoneal dialysis occur with similar frequencies.

Although the incidence of pruritus increases as renal function deteriorates, it does not improve with dialysis and is an independent marker of mortality at three years for those on hemodialysis. The severity of UP is associated with the duration of dialysis and xerosis. Unfortunately, the prevalence and burden of pruritus in end-stage renal disease (ESRD) is often underestimated by nephrologists, even though it is perceived by patients as a severe and distressing symptom of renal failure.

A study comparing half-body BB-UVB to whole-body treatments with varying dosimetry found a reduction in pruritus in 84 percent of patients treated with whole-body BB-UVB, with 29% not relapsing on an average of 10 month follow-up. Because patients did not detect a difference in the degree of pruritus between the half-body BB-UVB and placebo side, BB-UVB phototherapy was concluded to exert a systemic effect on UP secondary to the generalized response. The more intensive schedules accelerated the response temporarily but did not increase the percentage of patients who responded. In addition, the beneficial effects of UV exposure were only experienced after a lag time of two weeks in some patients. In another study, 80% of patients responded with complete relief of itching when treated with BB-UVB. Twenty-five percent of these claimed relief everywhere except for the palms and soles. All patients in this study had relief at least one month after therapy was discontinued, with 60% maintaining relief for at least six months. Cohen et al. reported that 57% of a series of pruritic patients experienced relief after BB-UVB therapy with a decrease in dermal mast-cell counts accompanying improvement in VAS scores. Finally, a case report by Hsu et al. found BB-UVB more effective than NB-UVB in decreasing pruritus in UP.

Discussion

Although pruritus is the most common chief complaint in dermatology, there are still many unknowns regarding its pathophysiology. Although classified into dermatologic, systemic, neurogenic, psychogenic, mixed, and other categories, this can help determine the etiology to address management options. Because objective measurements of pruritus are lacking, it is difficult to adequately assess and compare treatments; a uniform, consistent, and reliable scale of evaluating pruritus and scratching is needed. Nonetheless, based on current methodologies, which involve subjective evaluations, we have attempted to compare the different forms of phototherapy in treating pruritus.

Efficacy of Phototherapy in AD

Morison et al. published the earliest known reports of UV phototherapy for AD. This, combined with the general observation that pruritic patients improved during summer months, led to the use of phototherapy as a treatment modality for AD. As PUVA became integrated into the dermatologic practice in 1974, its long-term side effects of photo-aging began to limit its use in AD. UVA and UVB monotherapies were introduced in the 1980s, but had some downsides. UVB at times caused burning, xerosis, and erythema, although it required less time than UVA. UVB had a better therapeutic effect with light reactions, but with the drawback of lengthy procedure times. This led to the use of combination UVA/UVB therapy for AD. This was less time-consuming, decreased the total UV dose, and also minimized the risks of developing both short-term and long-term side effects.

NB-UVB is the modality of choice for AD when choosing phototherapy, as it is easily available in most dermatology clinics and is widely used for other conditions as well. BB-UVB is an alternative for those unable to tolerate the intense dosing of NB-UVB or in combination with UVA to increase efficacy. Despite the different doses, regimens, and clinical scoring systems used in the studies examined, UVA1 is a possible mode of treatment for AD. It is more suited for acute AD flares as it achieves results faster than UVAB and is more efficacious than either UVAB or topical corticosteroids. In addition, cold-light UVA1 is superior to UVA1 in reducing AD severity as it eliminates a potential trigger. Long-term follow-up reports are needed and further investigation is recommended to determine maintenance treatments. PUVA is also an option for AD. However, additional studies are needed to document its efficacy in treating pruritus.

Efficacy of Phototherapy in PN

NB-UVB is also the treatment of choice for PN, especially when combined with thalidomide to maximize the therapeutic potential of both treatment forms. BB-UVB is effective in treating PN as well, with a supportive reduction in pruritus. Although patients typically prefer topical PUVA over more painful treatment modalities such as intralesional steroid injections, BB-UVB was found to be more effective in treating cases of generalized PN and itch. Due to its more localized approach, MEL eliminates UV exposure to healthy skin. It is also more powerful than NB-UVB (TL01), thereby reducing the number of treatments required to reach remission. The advantage of weekly treatments as opposed to daily for topical treatments and phototherapy regimens also increases patient compliance in MEL. The use of combined synergistic therapies to reach remission is necessary in a chronic condition like PN, which requires similar UV radiation doses as psoriasis chronically to allow patients to undergo further phototherapy sessions. The use of UVA1 for PN treatment needs further investigation, although the studies we found thus far support its utility in treating PN. PUVA has also been
found beneficial in reducing not only pruritus but also the number of papules. PUVA also has a greater maintenance phase than other forms of phototherapy. Mild erythema is a possible side effect of all forms of phototherapy but quickly subsides. Mild hyperpigmentation at the lesional sites was common to most PN studies. Because of the longer wavelengths of UVA, it is potentially able to penetrate PN lesions better. Finally, the limited number of studies completed for the use of phototherapy in PN supports the use of UVB to decrease pruritus.

**Efficacy of Phototherapy in UP**

Even though NB-UVB is beneficial in decreasing GP and UP, it is less erythmogenic, has a lower pruritogenic potential, and is less carcinogenic than BB-UVB. BB-UVB is the treatment of choice for UP, while UVA is equal to placebo. In patients who are not candidates for kidney transplant, BB-UVB is considered the treatment of choice by some. While UVB radiation is safe, the risk for skin malignancies and long-term immunosuppression remains controversial in immunocompromised patients due to renal transplant. We did not find any studies on the use of PUVA in UP. Thus, more randomized, placebo-controlled trials are needed to determine the safest and most efficacious form of phototherapy for decreasing pruritus in patients on dialysis.

**Safety of Phototherapy**

Phototherapy is a safe form of treatment. When given long-term, PUVA has been associated with increased risk of cutaneous squamous cell carcinoma, but even high-dose exposure does not increase basal cell carcinoma risk. However, none of the published studies in a comprehensive review of BB-UVB and skin cancer risk demonstrates increased skin cancer risk, with one outlier of genital tumors in men receiving both PUVA and BB-UVB, thus necessitating the contemporary practice of genital shielding. A 25-year retrospective study looking at 280 psoriasis patients treated with BB-UVB and coal tar also did not demonstrate an increased skin cancer risk. A similar study conducted on 426 patients with atopic dermatitis and neurodermatitis treated with coal tar ointments and ultraviolet light (Goeckerman regimen) concluded that the incidence of skin cancer is not significantly increased above the expected incidence for selected populations in the United States.

**References**


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