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EVIDENCE-BASED REVIEW

Phototherapy for Pityriasis Lichenoides in the Pediatric Population: A Review of the Published Literature

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Abstract
Background Pityriasis lichenoides (PL) is a dermatologic disorder that manifests in either the acute (pityriasis lichenoides et varioliformis acuta) or the chronic form (pityriasis lichenoides chronica, also known as parapsoriasis chronica). Traditional first-line therapy consists of corticosteroids or antibiotics; however, these treatments are often accompanied with multiple side effects and may be ineffective.
Objective The goal of this study was to review the use of phototherapy for treating PL in the pediatric population.
Materials and methods We performed a systematic review of the literature in the National Library of Medicine's PubMed database and the SCOPUS database discussing phototherapy for treatment of PL in the pediatric population. The following search terms were used: 'pityriasis lichenoides', 'pityriasis lichenoides chronica', 'pityriasis lichenoides et varioliformis acuta', and 'febrile ulceronecrotic Mucha-Habermann disease'.
Results The systematic search and screening of articles resulted in 14 articles including a total of 64 patients with PL treated with phototherapy. Three different modalities were utilized, with five studies using broadband ultraviolet B (BB-UVB) radiation, nine studies utilizing narrowband UVB (NB-UVB), and two studies employing psoralen with ultraviolet A (PUVA) therapy. Overall, the use of BB-UVB had an initial clearance rate of 89.6 % with 23.1 % recurrence, whereas NB-UVB cleared 73 % of the lesions with no recurrence, and PUVA therapy initially cleared 83 % of the lesions with 60 % recurrence. The side-effect profiles were similar and revealed limited toxicity.
Conclusion Phototherapy shows promising results and a favorable side-effect profile in the treatment of PL. Ultimately, large randomized controlled trials are needed to determine optimal treatments.

1 Introduction

Pityriasis lichenoides (PL) is an uncommon dermatologic disorder that may manifest in two distinct forms: Pityriasis lichenoides et varioliformis acuta (PLEVA) and pityriasis lichenoides chronica (PLC), also known as parapsoriasis chronica [1, 2]. PLC is more common in children and young adults and generally emerges as a rash of small scaly red or brown papules [3]. In contrast, PLEVA lesions often present as pseudovesicles with central areas of necrosis [4, 5]. These conditions are relatively uncommon, with a collective incidence of 1/2000 people per year. PL is frequently associated with a younger patient population, as 20 % of PL cases occur in the pediatric age range [5].

Although the exact etiology is unknown, PLC is thought to be a T-cell-mediated reaction that may be precipitated by an acute infection [5]. Pathogens associated with this condition include *Toxoplasmosis gondii*, *Mycoplasma*, *Staphylococcus*, Epstein-Barr virus, cytomegalovirus, and parvovirus B19, among others [5]. In biopsy, an accumulation of cytotoxic T cells, immunoglobulin M, and C3 is often found in the involved tissue [5]. Given the suspected etiologies, first-line therapies often include topical or systemic corticosteroids, oral tetracycline, oral erythromycin, or other systemic antibiotics to both curtail an

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inflammatory response and treat an exacerbating infection. Unfortunately, PL may be unresponsive to these initial treatment modalities [5].

Light therapy has been used successfully to manage dermatological conditions such as psoriasis or vitiligo and is usually well tolerated [6]. It is thought that ultraviolet (UV) light may aid in the modulation of the immune response that may perpetuate the lesions seen in PL [5]. To this end, three phototherapy modalities are available. Broadband UVB (BB-UVB) utilizes light in the range of 280–320 nm for treatment. Narrowband UVB (NB-UVB) therapy uses a more limited spectrum of 311–313 nm, as it is thought that 311 nm is most effective in treating immune-related skin disorders [7]. A third available phototherapy option is oral or topical psoralen plus UVA (PUVA) [8]. Psoralens act as epidermal sensitizing agents that potentiate the therapeutic effects of the UVA spectrum ranging from 320 to 400 nm. When beginning therapy with any of these options, some providers use a minimal erythemal dose (MED) calculation to determine initial dose, which involves exposing an increasing area of skin to UV light over a given length of time with follow-up 24–48 h later [9]. Pityriasis demonstrates a more aggressive disease course in pediatric patients than in adults, with greater lesional distribution, more dyspigmentation, and a poorer response to conventional treatment modalities [10]. Investigation into additional therapeutic modalities is needed for this refractory disease. Although individual studies report the use of phototherapy for the treatment of PL in the pediatric population, no comprehensive review of its use has been performed. This study aims to evaluate the available literature on the use of phototherapy in the treatment of PL in the pediatric population and to discuss the clinical utility of this therapeutic modality.

2 Methods

We systematically searched the National Library of Medicine's PubMed database on 15 February 2016 for articles written in English related to laser and light therapy for PL in the human pediatric population aged <18 years. The following search terms were used: 'pityriasis lichenoides', 'pityriasis lichenoides chronica', 'pityriasis lichenoides et varioliformis acuta', and 'febrile ulceronecrotic Mucha-Habermann disease'. The search returned 657 articles. After titles and abstracts were screened for relevance, 39 papers were included for full-text review. Studies were included if they were original case reports, case series, or independent studies. Reviews and book chapters were excluded. Articles were excluded if information regarding clinical presentation or treatment was lacking, or where pediatric patients were not distinguished from adult patients within the same group. Therefore, 14 articles were included in this review. The search results were also cross-referenced with the SCOPUS database, which yielded no additional results. This article is based on previously conducted studies and does not involve any new studies on human or animal subjects performed by any of the authors.

The descriptions of treatment details varied widely between studies, meaning statistical analysis of the results presented a particular challenge. For each parameter evaluated, only studies that reported these measurements were included in amalgamations. Averages reported in each paper were weighted by number of patients involved in the study before being calculated in overall averages. Qualitative data, such as description of side effects, was simply identified as being present in patients of that particular study.

3 Results

The systematic search and screening of articles resulted in 14 articles discussing 64 patients with phototherapy-treated PL being included in the review (Fig. 1). Three different modalities were utilized, with five studies using BB-UVB radiation, nine studies using NB-UVB, and two studies using PUVA therapy. After 2007, the majority of studies reported (7/10) utilized NB-UVB as the phototherapy of choice ($N = 19/33$). Table 1 provides a summary of the overall treatment modalities, and the specifics of each study are detailed in Tables 2, 3, and 4, respectively.

To determine the initial dose, two studies calculated the MED [4, 12]. Three other studies used standard initial doses ranging from 100 to 200 mJ or tailored an initial dose to the patient's skin type [13–15]. Five studies used an increasing dose regimen, with an increase of 10–17 % or 0.01–2 J every session without erythema [4, 12, 14, 16, 17]. If erythema was noted, dose was decreased on the subsequent visit. One study [4] used three to five sessions per week; all others used three sessions per week. Therapy was universally well tolerated, with reported side effects consisting of mild to moderate erythema, burning sensation, and occasional pruritus [4, 12–15, 18, 19].

3.1 Broadband Ultraviolet B Therapy

BB-UVB therapy was a frequently utilized phototherapy option, accounting for five studies and 29 patients (Table 2). When reported, BB-UVB therapies included wavelengths in the 280- to 320-nm [20] spectrum within the included studies [4, 17]. An average of 21.1 treatments was given, with a range of 10–59 sessions [4, 10, 12, 17]. Total dose varied among studies and ranged from 0.8 to

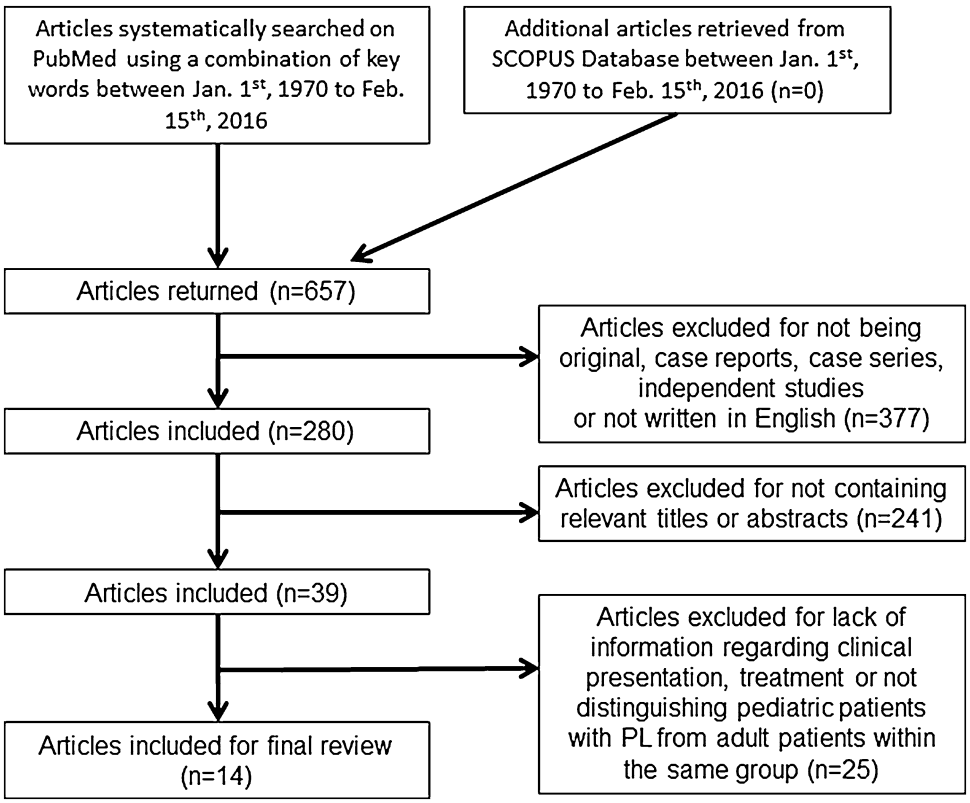

Fig. 1 Flow diagram of the literature identification and screening process. *PL* pityriasis lichenoides

Table 1 Summary of treatment modalities

Modality	*N*	Wavelength (nm)	Average No. of sessions (range)	Total dose (J/cm^2)	Initial clearance rate (%)	Recurrence rate (%)
BB-UVB	29	270–385	21.1 (18–33.3)	0.011–24.1	89.6	23.1
NB-UVB	29	309–313	18.8 (12–22)	3.023–301	73	0
PUVA	6	–	–	–	83	60

BB-UVB broadband ultraviolet B, *NB-UVB* narrowband ultraviolet B, *PUVA* Psoralen with ultraviolet A

11 J/cm^2 [10, 12, 17]. All but three of the patients treated with BB-UVB had initial clearance of the lesions (89.6 %) [3, 4, 10–12, 17]. Furthermore, these studies found a 20–50 % recurrence rate with BB-UVB therapy, with time of relapse occurring from 1 to 7 months after treatment completion [10, 17]. Three studies reported mild side effects of erythema, pruritus, and/or a burning sensation [4, 12, 17].

The first study [4] that used BB-UVB treated three patients with an average age of 6.7 years. These patients had previously been treated with topical steroids and oral erythromycin with unsatisfactory results and were treated with BB-UVB for an average of 33.3 sessions. Initial dose was established at 80 % of the predetermined MED and increased by 17 % each session without erythema. Phototherapy was given three to five times weekly until resolution was achieved, followed by a maintenance dose administered two to four times weekly. All three patients experienced complete resolution. Ersoy-Evans et al. [12] used BB-UVB to treat 12 patients with an average age of 9.9 years. These patients received an initial dose of 0.1 J/cm^2 that was increased by 0.01–0.03 J/cm^2 per treatment, for an average of 18 sessions. There was a clearance of lesions in ten of the 12 patients after an average follow-up of 3.7 months. A case study by Lane and Parker [3] detailed treatment of one 11-year-old child who had previously been treated with oral erythromycin for 6 months and fluticasone propionate ointment without success. The child showed initial improvement with BB-UVB therapy but was then lost to follow-up. A fourth case series by Tay et al. [17] discussed five patients with a mean age of 9 years. The lesions had been refractory to topical corticosteroids and oral erythromycin. Patients were exposed to BB-UVB spectrum over an average of 26 sessions. The dose was increased by 10 % each session, with total doses from 2.96 to 4.98 J/cm^2. Treatments were given three

Table 2 Broadband ultraviolet B in the treatment of pityriasis lichenoides

Study	*N*	Mean age (years)	Prior treatment	Lamp type	Wavelength (nm)	No. of Sessions	Dosing	Frequency (sessions per week)	Outcome	Adverse effects
LeVine [4]	3	6.7	Topical steroids, oral erythromycin	–	280 to 315	33.3	Initial dose of 80 % of the predetermined minimal erythema dose, increasing 17 % each session without erythema. Maintenance doses 2–4x every three weeks. Total dose range of 0.81–24.09 J/cm^2 (average of 11.03 J/cm^2)	3–5	Complete resolution	Erythema
Ersoy-Evans et al. [12]	12	9.9	–	UV 8001K cubicle with 27 UVA and 13 UVB fluorescent lamps	–	18	Initial dose of 0.1 J/cm^2 and increased by 0.01–0.03 J/cm^2 per treatment, total dose of 11 J/cm^2	–	Response in 10 (83.3 %) patients	Erythema, pruritus, burning
Lane and Parker [3]	1	11	Oral erythromycin × 6 months, fluticasone propionate ointment	–	–	–	–	–	Initial improvement, but patient lost to follow-up	–
Tay et al. [17]	5	9	Topical corticosteroids, oral erythromycin	Ultralite V4408 computerized phototherapy unit consisting of eight FS 72.TI2/ERE-HO UVB fluorescent lamps	270 to 385	26	Dose increasing by 10 % each session. Total dose of 2.96 to 4.98 J/cm^2	3	Initial clearance in all patients, 2 (40 %) patients had a single recurrence; 1 year follow-up	Erythema
Wahie et al. [10]	8	Specified as children	Topical corticosteroids, oral antibiotics	–	–	18	Total dose of 6.0 J/cm^2	–	Initial clearance in 7 (88 %) patients, 4 (50 %) patients had recurrence. 20 mo median follow-up	–

Table 3 Narrowband ultraviolet B therapy in the treatment of pityriasis lichenoides

Study	*N*	Mean age (years)	Prior treatment	Lamp type	Wavelength (nm)	No. of Sessions	Dosing	Frequency (sessions per week)	Outcome	Adverse effects
Brazzelli et al. [14]	5	10.4	Topical steroids and/or antibiotics	–	Peak emission of 311 to 313	–	Initial 100 or 180 mJ/cm^2, increased by 50 mJ/cm^2 increments	2–3	CR ($N = 5$) at 6 mo	Erythema and pruritus ($N = 1$)
Ersoy-Evans et al. [12]	5	–	–	45 Philips TL100W/01 fluorescent lamps and UV 8001K cubicle with 27 UVA and 13 UVB fluorescent lamps	–	22	Total dose of 9–301 J/cm^2	–	CR ($N = 5$)	–
Farnaghi et al. [13]	1	16	None	–	–	–	Initial 200 mJ/m^2 increased 10 % or decreased with adverse effects	3	>90 % clearance at 3 mo	Moderate erythema, burning sensation
Khachemoune and Blyumin [5]	1	14	–	–	–	20	–	3	CR at 1 yr	–
Koh et al. [18]	2	Pt. 1: 13; Pt. 2: 8	Pt.1: oral erythromycin, topical corticosteroids; Pt. 2: treatment naïve	–	–	Pt.1:13 Pt. 2: unspecified	–	–	Pt. 1: CR at 2 mo; Pt. 2: discontinued treatment at 1.5 mo	–
Nanda et al. [22]	1	12	Clarithromycin, IVIG, oral prednisolone, methotrexate	–	–	20	–	3 during the 1st 4 weeks, followed by a maintenance treatment (2 sittings per week × 3 weeks and 1 sitting per week × 2 weeks)	CR at 3 months	–
Pasic et al. [15]	9	11.5	Topical steroids, oral erythromycin	–	–	19	Cumulative dose of 3.023 to 11.8 J/cm^2	3	CR ($N = 3$), 70–90 % clearance ($N = 3$), or no change ($N = 3$)	Erythema
Someshwar and Udare [21]	1	2	–	–	–	–	–	–	"Good results"	–

Table 3 continued

Study	*N*	Mean age (years)	Prior treatment	Lamp type	Wavelength (nm)	No. of Sessions	Dosing	Frequency (sessions per week)	Outcome	Adverse effects
Tan et al. [16]	4	11	–	VS5 Series Phototherapy Booth with 56 (TL100/01) NB-UVB fluorescent lamps	309 to 313	–	Initial dose determined by skin type. Dose increasing by 10% each session without erythema	3	–	–

CR complete remission, *IVIG* intravenous immunoglobulin, *Pt* patient

times weekly. All five patients exhibited initial resolution of lesions, with two patients experiencing a single recurrence. Wahie et al. [10] followed eight patients in the pediatric age range. They were given an average of 18 treatment sessions and a total dose of 6 J/cm^2. Seven of eight patients had initial clearance, with four of these experiencing a recurrence of PL lesions after treatment with BB-UVB.

3.2 Narrowband Ultraviolet B Therapy

NB-UVB was used in nine studies, with 29 patients treated (Table 3); seven of these studies accounted for the majority of total studies (7/10) that were reported after 2007. An average of 18.8 sessions was needed to achieve results [5, 12–16, 18, 21, 22]. A reported wavelength of 309–313 nm was used [14, 16]. Total dose varied widely, ranging from 3.023 to 301 J/cm^2 [12, 13]. The 23 cases with sufficiently reported data demonstrated initial clearance in 74 % of cases (17/23), partial clearance in 13 % of patients (3/23), and no clearance in 13 % (3/23) [5, 12–15, 18, 22]. No recurrence of the lesions was seen in the three studies with longer follow-up (3 months to 1 year) [5, 14, 22].

Brazzelli et al. [14] used NB-UVB to treat five children with an average age of 10.4 years. These patients had been previously treated with topical steroids and/or oral antibiotics without resolution of the lesions. NB-UVB with a peak emission in the range of 311–313 nm was used. The initial dose was 100 or 180 mJ/cm^2, which was then increased by 50 mJ/cm^2 and given two to three times weekly. All five patients showed complete remission at 6 months. A second study by Ersoy-Evans et al. [12] used NB-UVB to treat five patients in the pediatric age range. An average of 22 phototherapy sessions was given, with total doses ranging from 9 to 301 J/cm^2. All patients showed a response to treatment, although no further details were given regarding full clearance, remission, or time to follow-up. Farnaghi et al. [13] reported treating a 16-year-old patient with treatment-naïve pityriasis lesions. The initial dose given was 200 mJ/m^2, which increased by 10 % after each session without adverse side effects. The patient was treated three times a week and had more than 90 % clearance. Likewise, Khachemoune and Blyumin [5] followed a single 14-year-old patient who was treated three times a week for a total of 20 sessions and experienced complete remission of the lesions at 1 year. Koh et al. [18] treated two patients with NB-UVB. One patient was a 13-year-old boy for whom treatment with erythromycin and topical steroids for 1 month had been unsuccessful. After receiving 13 sessions of NB-UVB over the course of 2 months, complete resolution was achieved. The other

Table 4 Psoralen and ultraviolet A therapy in pityriasis lichenoides

Study	*N*	Mean age (years)	Prior treatment	Lamp type	Wavelength (nm)	No. of Sessions	Dosing	Frequency	Outcome	Adverse effects
Ersoy-Evans et al. [12]	1	–	–	UV 8001K cubicle with 27 UVA and 13 UVB fluorescent lamps	–	–	–	–	No response	–
Romani et al. [19]	5	9.4	Topical corticosteroids, oral erythromycin	–	–	–	–	–	$N = 2$ (40 %) had CR at 2 months, $N = 3$ (60 %) relapsed. Two patients had 2 relapses and one patient had 4 relapses, that was controlled with methotrexate	No serious adverse effects

CR complete remission, *UV* ultraviolet

patient was an 8-year-old boy who had not received any prior treatment. The patient received an unspecified number of NB-UVB sessions. However, the patient defaulted treatment after 1.5 months and his outcome was unable to be determined. Another study [22] reported the use of NB-UVB combined with a 10-day course of prednisolone (0.5 mg/kg) for a 12-year-old boy. NB-UVB for 4 weeks at three sittings per week resulted in 100 % clearance. Maintenance treatment consisted of two sittings per week for 3 weeks and subsequently one sitting per week for 2 weeks. At 3-month follow-up, the patient continued to be in complete remission. Pašić et al. [15] used NB-UVB to treat nine patients with an average age of 11.5 years. Some had been previously treated with topical steroids and oral erythromycin without clearance of the lesions. Patients underwent an average of 19 treatment sessions, with a cumulative dose of 3.023–11.8 J/cm^2. Three of the nine patients had total clearance of lesions, three had partial clearance (70–90 %), and three had no change. Someshwar and Udare [21] described a 2-year-old patient who responded well to NB-UVB therapy but provided no details of dosing or follow-up. Finally, Tan et al. [16] treated four patients with an average age of 11 years with NB-UVB light in the 309- to 313-nm spectrum three times per week. Initial dose was determined by skin type, and dose was subsequently increased by 10 % each session without erythema. However, data regarding treatment efficacy in these patients was reported in combination with patients experiencing other skin disorders. Therefore, results for the four patients of interest to this paper cannot be reported.

3.3 Psoralen with Ultraviolet A (PUVA) Therapy

As expected, the use of PUVA was reported less often because of concerns about an increased risk of treatment-related secondary malignancy in patients aged <12 years [23]. Only two studies, treating a total of six patients (Table 4), were reported [12, 19], but the studies did not describe the total number of sessions and peak wavelengths. The six patients exhibited an 83 % initial clearance rate (5/6), with 60 % of these patients experiencing one or more recurrences (3/5). Of these, two patients had two relapses and a single patient had four relapses until achieving complete remission with methotrexate [13]. No serious adverse effects were reported, although long-term follow-up was lacking.

The first of the two studies utilizing PUVA is a case report by Ersoy-Evans et al. [12] in which one patient was treated using a UV 8001K cubicle with 27 UVA and 13 UVB fluorescent lamps in conjunction with an unspecified dose of oral psoralen. This patient had no resolution of the lesions. A case series by Romaní et al. [19] followed five patients with a mean age of 9.4 years. All five patients had initial clearance of the lesions after 2 months of PUVA therapy; two children experienced two relapses, and a third experienced four relapses, with eventual resolution of symptoms after treatment with methotrexate.

4 Discussion

The majority of the patients responded well to the phototherapy modalities, though a portion of patients had recurrent disease after therapy. Less recurrence was seen in UVB-treated cases than in PUVA-treated cases, with NB-UVB therapy demonstrating the lowest recurrence rate. This difference may be because, of the three modalities, only the 311-nm wavelengths used in NB-UVB therapy have excellent penetration into dermis and the epidermis, leading to more complete apoptosis of offending T cells [24]. Long-term effectiveness is an important consideration when treating this often refractory disease, so NB-UVB therapy provides a promising treatment option.

Side-effect profiles of all three modalities were comparable and reportedly minimal. Erythema, pruritus, and discomfort or pain were the most commonly observed toxicities. The high number of sessions and frequencies of treatment reported—up to thrice weekly in most studies—is a considerable factor in delivering care and is also a potentially large burden on the patient. However, all except two studies [4, 12] selected a standard initial dose or an initial dose based on skin type, as opposed to determining the MED. While the former method is far more time intensive, it could potentially reduce the number of sessions required by allowing a higher starting dose for phototherapy. Another factor to consider with the use of these therapies, particularly with PUVA, is the associated risk of developing secondary malignancy. Cases of squamous cell carcinoma and melanoma have been reported in adults previously treated with PUVA [25–28]. There has been concern that exposure during a 'critical period' in young childhood may compound this risk, although a study by Pfahlberg et al. [29] found no such association. However, more study of the risks associated with phototherapy is still needed in the pediatric population, and the long-term risk of toxicity should be considered in younger patients [25, 30].

In numerous studies, phototherapy was not the first-line treatment choice. Of the ten studies discussing prior treatments, nine reported initial use of topical and systemic corticosteroids, and eight reported the use of oral antibiotics [3, 4, 10, 12–15, 18, 19, 22]. One patient received methotrexate 5 mg and intravenous immunoglobulin for 2 days without success [22]. Additionally, only one study [4] reported using maintenance doses after lesion clearance. While insufficient evidence precludes determination of maintenance dose efficacy, further investigation is warranted given the high recurrence rate of this disease. Considering the excellent side-effect profile of phototherapy reported in the included studies, the use of first-line combination therapies involving phototherapy in conjunction with traditional pharmacological treatment may have potential as a therapeutic approach and should be investigated further.

5 Conclusion

Overall, studies investigating phototherapy approaches to the treatment of PL are limited by their low power and short follow-up times. Given the efficacy and limited acute side-effect profile suggested by the available literature, future larger studies are warranted to determine the role of phototherapy in the treatment of PL. As such, data indicate light therapy could be a promising treatment option in pediatric patients with this often persistent and refractory disease.

Compliance with Ethical Standards

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All named authors meet the International Committee of Medical Journal Editors (ICMJE) criteria for authorship for this manuscript and take responsibility for the integrity of the work as a whole. All authors have given final approval for the version to be published.

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