Phototherapy in Pediatric Dermatology

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ABSTRACT

Background: Phototherapy is a safe and effective treatment modality for skin diseases in children such as psoriasis, atopic dermatitis, pityriasis lichenoides, vitiligo, cutaneous cell lymphoma, pityriasis rubra pilaris, and other skin disorders. It is reported to be effective with less side effects compare to the administration of systemic medicine. Short and long term side effects should be taken into account when applying this model of therapy, especially in children. **Purpose:** To identify special considerations regarding the use of phototherapy modalities in the field of dermatology in children. **Review:** Phototherapy is the use of ultraviolet (UV) radiation for therapeutic purposes. The various wavelengths of UV radiation used for phototherapy have their own respective photochemical and photobiological properties. There are modality choices that have been proven to provide benefits in treating various skin diseases, including broadband UVB and narrowband UVB, psoralen UVA photochemotherapy (PUVA), ultraviolet A 1 (UVA1), and targeting phototherapy. Special considerations regarding the use of this treatment modality in the pediatric population increase with safety and treatment tolerance. **Conclusion:** Special considerations should be taken when providing phototherapy treatment options to children with skin disorders requiring phototherapy. The therapies are generally well tolerated and mostly have minor adverse side effects, such as sunburn.

Keywords: Children, phototherapy, treatment, human and medicine.

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BACKGROUND

Phototherapy is a form of therapy with the provision of ultraviolet (UV) radiation with certain wavelengths to treat various dermatological conditions. In contrast, photochemotherapy is a combination of UV radiation and photosensitizer (for example, psoralen).[1] Phototherapy has become one of the commonly used modalities for treating various skin diseases in adults. Phototherapy can also be a safe and effective treatment for various skin diseases in children (newborn, child, and adolescent).[2] Phototherapy is reported to be effective with less side effects compare to the administration of systemic medicine. Side effects of short term phototherapy including erythema, burning, pruritus, and xerosis, which usually arise and are temporary. The long term effects of primary concern are premature aging of the skin and increased carcinogenesis. When considering phototherapy treatment for children, the most common concern experienced by doctors is the risk of long term carcinogenesis.[3] Special considerations should be taken when applying this therapeutic model, especially to children. Specific considerations regarding the need to use this treatment modality in the pediatric population including patient, family, and facility factors, which have strong concerns for the safety and tolerance of treatment.[4]

REVIEW

Phototherapy means the use of UV radiation for therapeutic purposes. Ultraviolet radiation is used in phototherapy to treat skin diseases, either single therapy or in combination with other drugs.[1] The beneficial effects of phototherapy in these inflammatory skin conditions are largely through anti-inflammatory and immunomodulatory effects on lymphocyte T cells, proinflammatory cytokines, and presentation of Langerhans cell antigens.[2] The key role of wavelengths is a consequence of the basic law of photobiology which states that light must be absorbed to initiate physical, chemical, or biological effects.[4]

Ultraviolet spectrum is divided into three ranges based on wavelength, namely UVA (320–400 nm), UVB (290–320 nm), and UVC (200–290 nm). The UVA spectrum is further divided into UVA1 (340–400 nm) and UVA2 (320–340 nm).[4] From these wavelengths, there are several phototherapy modality options, including broadband UVB (BBUVB) and

narrowband UVB (NBUVB), psoralen ultraviolet A (PUVA), ultraviolet A 1 (UVA1), and targeted phototherapy. Special consideration is needed in prescribing phototherapy to children, including evaluations for newborns, children, and adolescents, related risks, treatment strategies at the clinic, and treatment strategies at home.[2,3]

Each wavelength of UV radiation used in phototherapy has its own photochemical and photobiological properties, including differences in penetration depth and distance of molecules in interacting skin. Consequently, each form of phototherapy has unique properties with potential effects, side effects, and optimal use for certain diseases.[3,5] Ultraviolet B radiation has a wavelength of 290–320 nm. Most of the UVB radiation is absorbed by the epidermis and superficial dermis. In contrast to UVB radiation, which has a relatively superficial penetration depth, UVA radiation has a 320–400 nm wavelength, reaching the middle or lower dermis. In PUVA photochemotherapy, psoralen photosensitizers are activated by UVA radiation, and the depth of PUVA penetration is in the mid dermis. The effects of phototherapy on the patient's body with skin negligence, including its effect on the immune system, mast cells, collagen, epidermis, and melanocytes.[3]

In general, the initial doses of BBUVB and NBUVB are determined in one of two ways. The first method, the minimal erythema dose (MED) is determined by exposing 6 areas sized 1 cm^2 on the inner aspect of the arm or forearm, gradually increasing UV radiation from the same device to be used for phototherapy. Twenty four hours later, the areas exposed to the UV rays will be examined and the smallest UV dose that produce uniform erythema across the area is considered MED and phototherapy is started at 50% to 70% of that amount. The second way, the initial dose of phototherapy is determined empirically on the Fitzpatrick's skin phototype. Subsequent exposures are given 2–5 times per week and the dose is increased with each treatment. If an erythema response has occurred, then, depending on the severity, the dose is reduced, or treatment interval is delayed. The maximum dose of NBUVB is 2,000–5,000 mJ/cm^2, depending on the photoreactive skin type. If the patient misses a treatment, dose modifications should be made to avoid burns.[3]

Psoralen UVA photochemotherapy combines oral ingestion or topical application of psoralen with exposure to UV radiation in the UVA range. Three forms of psoralen are used in the photochemotherapy regimen: 8-methoxypsoralen (8-MOP), 5-methoxypsoralen (5-MOP), and 4,5, 8-trimethylpsoralen (TMP). In the United States, only 8-MOP is available. There are two oral formulations of 8-MOP, the micronized form, which is usually administered at a dose of 0.6 mg/kg 120 minutes before UVA exposure, or the dissolved form given at a dose of 0.4–0.6 mg/kg 90 minutes before UVA exposure. For oral PUVA therapy, UVA radiation is usually initiated at doses that are appropriate to 50%–70% of the minimum phototoxic dose (MPD) or according to Fitzpatrick's skin phototype.[3]

Ultraviolet A 1 (UVA1) has a wavelength of 340–400 nm. It can penetrate much deeper into the skin than UVB or a shorter range of UVA called UVA2, which is 320–340 nm. Ultraviolet A 1 is given 3–5 times per week. Several studies have attempted to determine the optimal amount of UVA1 for each treatment session. Three dosage regimens that have been used are (1) low dose (10–30 J/cm^2), (2) medium dose (40–70 J/cm^2), and (3) high dose (130 J/cm^2). Although several comparative studies have been conducted, at this point, there is no consensus on the dosage. In general, patients are started at 20–30 J/cm^2 and increased to the full dose of 3–5 treatments. The risk of burns is much less than that of UVB or PUVA therapy.[3]

The targeted phototherapy devices include excimer lasers and non laser devices known as monochromatic excimer light (MEL) devices. In contrast to the phototherapy devices described previously, which expose the skin to a large extent, targeted phototherapy provides a therapeutic dose of UV radiation only to skin lesions. The handheld form of targeted phototherapy devices may be easier for children than receiving treatment in a phototherapy booth, which can be overwhelming and intimidating. The limitations of the targeted phototherapy include a higher cost for the device and impractical to cover more than 10% to 20% of the body surface.[3]

Special considerations are needed in prescribing phototherapy to children, including multifactorial processes and involving both the parents and patient. Thorough evaluation of the history of the disease, previously failed treatment therapies, and effects on quality of life should also be considered. Narrowband UVB is preferred for children over PUVA for almost all skin conditions due to the side effects of PUVA, which can cause phototoxicity, carcinogenesis, photoaging, cataracts, and a more permeable eye lens at a younger age. Therefore, PUVA is a relative contraindication in children younger than 12 years. Age at initiation of therapy depends on the type of phototherapy and the cost of conventional policies rather than data based guidelines. Reasonable school age children are considering starting UVB therapy, but candidates for younger pediatric patients may be able to reconsider. The appropriate development of

children's attitudes and emotions, negative images of separation, fear of closed spaces, and the ability to remain silent during treatment.[1,2]

Absolute contraindication to phototherapy is negligence induced by both acquired and inherited UV light such as erythematous lupus, dermatomyositis, xeroderma pigmentosum, porphyria, and basal cell nevus syndrome. A history of polymorphic light eruptions will require a gradual increase in exposure but is not an absolute contraindication to phototherapy. Medications should be studied to identify drugs that make them photosensitive; in children, this is often found in antibiotics, antidepressants, anticonvulsants. Treatment may present relative contraindications to phototherapy, but a reduction in the phototherapy dose may also be considered. A family history of skin cancer should be explored, although it is not contraindicated.[2]

Psoriasis is a chronic, immune-mediated inflammatory disease of the skin, affecting the skin, nails, and joints in both children and adults. Psoriasis begins in childhood in nearly one third of cases.[4] In psoriasis, cells that present antigens (dendritic cells and macrophages) activate naive T helper (Th) cells and induce their differentiation into Th1 and Th17 cells, leading to the release of Th1 and Th17 cytokines that promote inflammation and epidermal hyperplasia. Phototherapy has been shown to decrease Th1/ Th17 regulation and the proinflammatory axis and improve regulation of the Th2 pathway, which leads to clinical improvement. There are four mechanisms of action to explain the effects of phototherapy on psoriasis, namely working by changing cytokine profiles, inducing apoptosis, promoting immunosuppression, and other mechanisms.[6,7]

Phototherapy for the treatment of psoriasis begins with the emergence of BBUVB, NBUVB, PUVA, and laser treatment modalities. Pediatrics and pregnant patients represent a subset of the population that requires extra testing before phototherapy administration. Phototherapy is safe and effective as a second line treatment option for pediatric patients who are not responsive to topical therapy.[7,8] Phototherapy is an effective treatment for pediatric patients with psoriasis. Narrowband UVB (311–313 nm) is the most frequently studied and administered because it has a relatively good safety profile, efficacy, and ease of administration. In the most recent and largest study involving 88 pediatric patients with psoriasis, the average age of 12 years ± 4 years received NBUVB therapy for 3.1 ± 2.26 months with a cumulative average dose of 46.5 J/cm^2. Overall, 92% of children treated with NBUVB had an increase of more than 75%, with the full value found in 51% of the population. This response value is almost similar to the previous retrospective cohort studies.[2] Other treatment modalities are BBUVB (290–320 nm) and UVA (320–400 nm) with topical or systemic psoralens. In a series of 30 patients with psoriasis (mean age 11± 3.6 years) treated with BBUVB (average number of treatments 28.8 ± 13.3), 93.3% of participants received an increase of more than 75%. Seven patients with plaque or guttate type psoriasis were treated with PUVA and over 75% improvement in 83% of patients with a mean PUVA treatment of 28 times.[2]

Phototherapy regimens involving adjuvant therapy with other topical and systemic drugs have also been studied with mixed results. Topical agents have efficacy in patients receiving phototherapies such as serous emollients (such as mineral oil), topical corticosteroids, vitamin D analogs (should be given after phototherapy), charcoal, or topical retinoids. However, topical salicylic acid may decrease the efficacy of phototherapy. Systemic retinoids have been reported to increase the efficacy of UV therapy, whereas methotrexate should be given with caution as it increases the risk of photosensitivity.[2]

Phototherapy is a safe and effective second line treatment option for pediatric patients who are unresponsive to topical therapy.[8] Phototherapy is considered a safe and effective treatment for children who can follow the protocol of phototherapy. Although phototherapy is a simple and natural way of treatment, both the children and parents must be educated about the hazards of overexposure.[6]

Atopic dermatitis (AD), also known as atopic eczema, is a common inflammatory skin disease characterized by a chronic and relapsing course.[9] This disease usually appears in infancy or childhood and may persist into adulthood. Together, genetic and immunological factors contribute to skin barrier dysfunction and play a major role in the pathogenesis of AD.[10] Phototherapy should be considered second line therapy for pediatric patients with moderate or severe atopic dermatitis.[2]

Various phototherapy modalities have been studied, including BBUVB, NBUVB, UVA, UVA1, PUVA, and a combination of UVA and UVB. A recent consensus by the American Academy of Dermatology states that UVA and UVB are effective treatments and well tolerated for children with AD, either as monotherapy or in combination with emollients or topical steroids.[2,9] There is strong evidence to support the efficacy of phototherapy in the pediatric patient population with AD. In general, NBUVB is the preferred modality for the treatment of AD in a pediatric population.[2,10]

A retrospective study by Clayton *et al.* involving 50 children with AD using NBUVB showed a complete

remission or minimal residual activity in 40% of patients, a good improvement in 23%, and a moderate increase in 26%. In a systematic review of phototherapy in treating AD, Meduri *et al.* reported three studies that found the response to UVA1 was faster and more effective than combined UVA and UVB phototherapy. In contrast, two trials reported the advantages of UVA and UVB. The review founds two additional studies that showed that NBUVB was more effective than BBUVB or UVA for chronic AD. A further study by Pavlovsky *et al.* reviewed 72 children with AD who had undergone NBUVB, 25% achieved total remission, and another 44% had a partial response.[10] The mechanism of UV light in the treatment of AD has not been fully explained. In a recent study, it was said that the effect of NBUVB on epidermal cells was able to induce apoptosis of Langerhans cells and T-cells, reduce the number of keratinocytes, and promote accelerated cell migration, wound healing, and repair of the barrier. Ultraviolet B radiation has also been shown to suppress proinflammatory cytokines, such as interleukin 12 (IL-12), IL-2, interferon-alpha, tumor necrosis factor-alpha, and increase keratinocytes IL-10 production, a strong inflammatory cytokine suppressor. Administration of NBUVB has also been shown to increase the expression of antimicrobial peptides such as beta-defensin and catelidine and increase levels of calcitriol, which has an immunomodulatory effect on keratinocytes and T-lymphocytes.[11,12]

Phototherapy represents an optimal resource for the treatment of AD. Phototherapy can reduce disease burden in severe eczema and therefore should be considered second line therapy after standard topical regimens have failed. Its use is generally considered safe and it is well tolerated. However, some short term and long term adverse effects have been described, and the risk of carcinogenesis has not been excluded. Therefore, phototherapy must be used conscientiously, especially in children.[9]

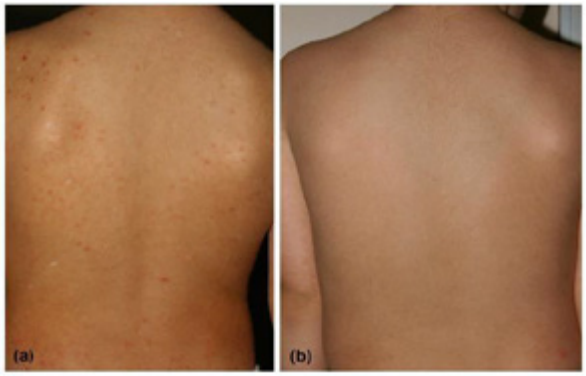
Pityriasis lichenoides (PL) is a rare skin disorder, characterized by a spectrum of clinical manifestations ranging from early papillary acute papules such as *pityriasis lichenoides et varioliformis acuta* (PLEVA) to brown papules such as *pityriasis lichenoides chronica* (PLC). The PL incidence is estimated to be around 1 in 2000, and 20% of cases affect children, with peak events around 5 and 10 years of age.[13] The exact mechanism of action of phototherapy in the PL is unknown. However, all of them modulate inflammation and immunological activity of the skin through different photobiological mechanisms of action from each other. Specifically, NBUVB reduces T cells in inflamed skin lesions and has a direct cytotoxic effect on T cells infiltrating skin lesions. Recent research has shown that UVB suppresses self activation and the presentation capacity of Langerhans cell epidermal antigens and modulates interleukins (IL-1, IL-6, IL-8, IL-10, IL-12) and tumor necrosis factor-α production by human keratinocytes. Modulation of circulating cytokines contributes to systemic induced NBUVB immunosuppression. Furthermore, UVB irradiation has been found to suppress the expression of intercellular adhesion molecules.[1]

Psoralen UVA phototherapy was preferred for patients with the more widespread or long evolving disease, while UVA/ UVB was selected for patients who presented more recent disease or contraindications for PUVA therapy. Regardless of the absence of clinical guidelines, both therapeutic options proved to be successful, ascertaining phototherapy as an effective and safe option for PL patients.[14] Narrowband UVB phototherapy is a therapeutic modality with a well known efficacy and safety profile, which makes it especially suitable for the treatment of childhood skin diseases. The effect of NBUVB as an antiinflammatory and induces immunological changes can be part of the immunotherapeutic role of NBUVB in the PL and its role in preventing the recurrence of the disease. Furthermore, NBUVB is considered a safe and effective therapeutic option even in the pediatric population.[13,14]

A study of 5 patients (2 with PLEVA and 3 with PLC) with PL treated with NBUVB reported complete remission in 5 patients after therapy with averaging 21 sessions (range 13 to 40 sessions), together with a mean duration of therapy of 4 months (range 2 to 8 months. The average cumulative dose was 21 J/cm^2 (range 15–32 J/cm^2). Each patient was maintained in the remission phase from illness at 3 months and 6 months visit.[2] There was no benefit from proven phototherapy as adjunctive therapy from systemic drugs such as corticosteroids, antibiotics, and antihistamines. A study involved 70 patients with a mean age of 25 ± 18 years (range from 2 to 80 years) treated with phototherapy, comparing the clinical effectiveness of NBUVB phototherapy, systemic therapy, and the combination of both.[2,13] Based on the complete disappearance rate of 90% in cohorts handled with NBUVB alone, monotherapy using NBUVB was an effective and well tolerated way of eliminating the need for accompanying systemic drugs, 81.1% of patients treated with NBUVB experienced relapse free in the first 20 weeks and this result was obtained in all groups including the pediatric patient population.[2,14]

Although the exact mechanism of phototherapy in PL remains unknown, it represents a valid therapeutic modality for these patients. The present study indicates

that PUVA and UVA/ UVB are successful and safe modalities. Additional data, especially from studies performed to compare other treatments with phototherapy and studies about maintenance therapies for PL are needed.[14]



Picture 1. Before (a) and after (b) treatment using phototherapy in patients with Pityriasis lichenoides**.**[13]

In contrast to non-Hodgkin nodal lymphoma, which is mostly B-derived cells, 75% of primary skin lymphoma is derived from T cells, two-thirds of which can be classified as Mycosis fungoides (MF) or Sezary Syndrome (SS).[15] Mycosis fungoides is the most common form of cutaneous T-cell lymphoma (CTCL). It is estimated that 0.5–5% of cases develop during childhood, with the patch stage disease being the commonest stage of presentation in the pediatric age group. The diagnosis of MF in childhood is often delayed due to its rarity and its propensity to mimic other inflammatory dermatoses, both clinically and histologically.[16,17]

Treatment strategies for children with MF must be made on a case-by-case basis, evaluating multiple factors, including the patient's ability to cooperate with treatment, patient and family expectations, and side effects of treatment.[17,18] There are several options available for MF treatment, including topical therapies, systemic therapies, and phototherapy.[16] The European Organization for Research and Treatment of Cancer (EORTC) guidelines suggest that appropriate first line therapies include observation only, PUVA, UVB (patches only), topical corticosteroids, radiotherapy, total skin electron beam therapy, mechlorethamine, and carmustine.[18]

Phototherapy has been used as a first line treatment for the management of MF in both children and adults. The study supports the role of phototherapy in the treatment of stage IA and IB disease.[16,18] The success rate with PUVA is 90% for stage IA, 76% for stage IB, 78% for stage IIA, 59% for stage IIB%, and 61% for stage III CTCL. The most commonly reported acute side effects are erythema, pruritus, and nausea. Long term exposure is associated with an increased risk for developing photodamage and nonmelanoma skin cancers. The latest consensus from EORTC shows that patients with patches and thin plaques should be given NBUVB treatment. In contrast, PUVA should be provided for patients with folliculotropic MF, failure of NBUVB therapy, or dark skin, because of carcinogenic effects and the lack of available treatment centers.[2]

Recent retrospective research establishes that PUVA and NBUVB are effective treatments for stage I CTCL in pediatric patients, with a tendency to NBUVB due to relatively better ease of administration.[2,18] Although NBUVB therapy has been used mainly for patch stage MF, PUVA has been used in both patch and plaque stage disease.[16] Psoralen UVA would appear to provide a longer period of remission with less frequent attendance (twice weekly), whereas NBUVB may achieve shorter periods of remission and require more frequent attendance (three times weekly) with a lower photocarcinogenic effect.[18]

The choice of treatment largely depends on availability, patient history (in terms of earlier treatment responses), and physician experience. It is a widely accepted consensus that patients with patches and thin plaques NBUVB should be preferentially used and that PUVA should be reserved for patients with thick plaques (including follicular mucinosis) with phototypes ≥ III and insufficient response to UVB.[18]

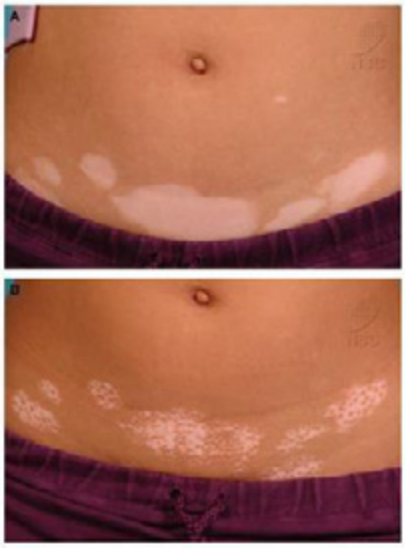
Vitiligo is a depigmented disorder that affects about 1% of the world's population. About 50% of cases have onset before 20 years and 25% before the age of 14 years. Vitiligo is characterized by selective damage from the basal melanocytes of the epidermis and/ or sometimes hair follicles, producing white patches on the skin, mucous membranes, and/ or hair. Various theories have been put forward for the etiology of vitiligo, including genetic, neurological, autocytotoxic or metabolic, and autoimmune theories, all of which are included in convergence theory.[19,20] Vitiligo has a multifactorial etiology, in which genetic factors, various kinds of stress (emotional stress, oxidative stress with accumulation of free radicals), the accumulation of toxic melanin precursors in melanocytes (for example, 3,4 dihydroxyphenylalanine and 5,6 dihydroxyindole), melanocyte homeostasis disorders (for example, intracellular disorders and extracellular calcium), and autoimmunity can contribute to the development of the disorder. Vitiligo is often associated with various organ specific autoimmune diseases, such as Hashimoto's thyroiditis, Addison's disease, type 1 diabetes mellitus, and pernicious anemia. Hashimoto's thyroiditis is the most common relationship in children. This finding is

important regarding the management of children with vitiligo.[20,21]

Minor differences in the management of childhood versus adult vitiligo are mostly because of feasibility and aesthetic demand of treatment. The major difference comes from the parent's response and coping with the disease, especially in vitiligo families. Early intervention, regardless of the vitiligo type, is preferred to limit disease extension. However, the benefits/risks of the treatment should be weighed cautiously in terms of the time needed to apply topicals or more importantly in case of deciding for phototherapy.[19] Koh *et al*. (2015) recommended phototherapy in pediatric patients with vitiligo who did not respond to topical drugs with extensive involvement of body surface area or the disease had gotten worse. In this study, as many as 71 vitiligo patients aged 5 to 15 years with skin types IV to VI treated with these various modalities had a good response rate of 74% with NBUVB (14/19), 67% with a combination of UVB or UVA1 (26/39), 54% with excimer laser (10/19), and 53% with topical PUVA (13/25). Therefore, NBUVB is the most opted and studied therapy for vitiligo. Despite the obvious clinical efficacy, the underlying mechanism is unclear. However, the latest literature mentioned influencing T-regulator cells (Tregs) and antioxidant oxidation theory.[2,21]

Research in Indonesia shows that NBUVB exposure 2–3 times a week in a row for 6–12 months results in > 75% repigmentation in at least 50%–75% of children. The response to treatment depends on the location, area, duration of vitiligo, and duration of treatment. Children with the latest vitiligo and/ or lesions located on the face and neck have a better response to therapy. Unlike NBUVB phototherapy, a 308 nm excimer laser device delivers radiation to the vitiligo skin only indicated for local vitiligo. However, it is time consuming and may interfere with childhood activities, including school attendance.[20,22] Heliotherapy (natural exposure to UV light) is an alternative therapy, but it should be carried out in care to prevent excessive sunburn.[20] Vitiligo treatments, especially in children with lighter skin types, are often delayed. Early vitiligo treatment for both skin types is encouraged for better results. This treatment is applicable to younger children. Some groups recommend stopping treatment after 6 months if it is ineffective in limiting the overall cumulative dose and reducing the risk of future malignancy. Excimer UVB is recommended for limited body surfaces resistant to NBUVB in general or for areas requiring focal higher doses. Topical PUVA should be considered for local resistant plaque that is not responsive to other therapies.[2,23]

A retrospective study in 2015 by Bae *et al*. involving 159 patients with segmental vitiligo aged from 1 to 62 years treated with a 308 nm excimer laser combination, topical tacrolimus, and short term corticosteroids having at least 75% repigmentation in 50.3% of patients after a median duration of treatment 12.1 months. These results suggest that combination therapy may be an effective approach in patients with challenging conditions, refractory disease subtypes.[23] In conclusion, NBUVB may be a safe and preferred treatment option for children because it is generally well tolerated with minimal side effects. PUVA is also a treatment option for vitiligo as the second line because of potential increased skin cancer risk. Therefore, NBUVB is preferred to PUVA.



Picture 2. Vitiligo patients. Before (A) and after (B) treatment using phototherapy.[18]

Pityriasis rubra pilaris (PRP) is a rare papulosquamous inflammatory disorder with an unknown etiology. The pathogenesis of PRP remains unclear, although several prominent hypotheses exist, including dysfunction in keratinization or vitamin A metabolism, autoimmune mechanisms, triggers of abnormal immunology, such as infection or UV exposure. Genetics seems to play a role in the development of at least a few cases of PRP, most notably noted in the type-V of PRP. A clear association with gain-function mutations in Caspase Recruitment Domain Family Member 14 (CARD14), also known as susceptibility psoriasis (PSOR2), is a gene that codes for member 14 protein, an activator of Nuclear Factor-kappa beta. Incidentally, similar mutations have been noted in patients with sporadic PRP. Further research is needed. Human immunodeficiency virus (HIV) has been linked to the development of type-VI PRP.[24,25]

In many cases, PRP is a self limiting and

asymptomatic disease because it does not need treatment. Standard treatment guidelines for PRP are lacking. Therapeutic options including vitamins, retinoids, antimetabolites, immunosuppressive agents, antibiotics, UV phototherapy, biological agents, and fumarate acid. Most practitioners recommend topical combination therapy for symptom management and systemic therapy aimed at reducing inflammation. Although the risk of UV light therapy has been implemented in certain cases, including NBUVB, UVA1, or PUVA in combination with oral retinoids with some success.[24,26] Combined UVA1 radiation and acitretin therapy may be an alternative treatment, but phototesting must be done before treatment because of reports of PRP being exacerbated by light. Kaskel *et al.* reported that patients with papules and infiltration prescribed with UVB (0.04 J/cm^2) developed general PRP 4 days after irradiation. The same patient was then successfully treated with PUVA baths. Oral retinoids and photochemotherapy with methoxsalen 8-MOP PUVA may be good treatment options. The initial UVA dose should not exceed 0.3–0.5 J/cm^2 with the subsequent addition of 0.3 J/cm^2 every third day. Davidson *et al.* reported, in a series of examinations of 57 PRP patients, of which 26% showed exacerbations in the summer months. A 12 years old girl with a 4 years history of PRP was successfully treated with NBUVB in combination with acitretin starting at a dose of 0.75 mg/kg/day. Acitretin can cause relapse in areas protected from light, such as axilla, yet it is not completely clear. The authors suspect that NBUVB has a different biological effect from BBUVB; for example, more immunosuppressive effects on lymphoproliferation and cytokine responses of peripheral blood cells. However, different response rates with phototherapy seem to reflect the heterogeneity of PRP because some patients show improvement with light therapy and others experience exacerbations.[24]

Other diseases successfully treated with phototherapy in pediatric patients are urticaria, alopecia areata, localized scleroderma disease, morphea, nodular prurigo, Langerhans cell histiocytosis, graft versus host skin disease, and herpetiformis dermatitis.[27] Phototherapy is rarely recommended but can be prescribed if the first, second, and even third treatment options fail. Phototherapy has also been used to eliminate the manifestations of light sensitive skin eruptions, such as erythropoietic protoporphyria and polymorphic light eruptions. Manifestations such as photoprophylaxis or hardening of the skin have been reported to increase in sunlight tolerance in patients receiving this treatment. Phototherapy may be considered prophylactic in other dermatological conditions that are known to be sensitive to light.[2]

DISCUSSION

Phototherapy means the use of UV radiation for therapeutic purposes. Ultraviolet radiation is used for phototherapy in skin diseases, either alone or in conjunction with other drugs. The benefits of phototherapy in inflammatory skin conditions are largely through antiinflammatory and immunomodulatory effects on T-lymphocytes, proinflammatory cytokines, and the presentation of Langerhans cell antigens. Each wavelength of UV radiation has its own photochemical and photobiological properties. Consequently, each form of phototherapy has unique properties with potential effects, side effects, and diseases in which they are effective. Phototherapy will give effect to mast cells, collagen, epidermis, and melanocytes.[1,2]

Wavelengths in phototherapy are BB UVB, NB UVB, UVA1, PUVA, and targeted phototherapy. Special considerations must be applied when trying to provide phototherapy for children with neglected skin. Evaluation of children and adolescents should begins with exploring a thorough history, including determination of disease complaints, previous treatments that failed, and effects on quality of life. It also needs to be considered related to side effects that can arise. It is also important to know treatment strategies at the clinic and home.[3]

The success of phototherapy in adult and child populations has been widely discussed. There are several cases of skin neglect in children as an indication of phototherapy, namely psoriasis, AD, PL, vitiligo, cutaneous cell lymphoma, PRP, and other skin disorders. This therapy is generally well tolerated and mostly has mild adverse side effects. Reactions such as sunburn are the most common adverse effect of short term phototherapy.[2] Summary of conditions for which phototherapy is used seen in table 1.

Table 1. Summary the used of phototherapy.[28]

NB-UVB	*UVA$_1$*	*PUVA*
Psoriasis	Morphea	Psoriasis
Atopic dermatitis	Atopic dermatitis	Atopic dermatitis
Vitiligo		Vitiligo
Mycosis fungoides		Mycosis fungoides

This literature recommends safer treatment for children in accordance with the skin conditions such as psoriasis, AD, and vitiligo. However, further prospective research is needed to understand the long term risks of these therapies, especially in children. These therapies can be prescribed along with other topical and systemic therapy as a combination therapy. Short term adverse effects from all types of phototherapy can include burning, erythema, xerosis,

and pruritus, which are usually transient, mild, and well tolerated. The long term effect includes increased potential risk of carcinogenesis, but further study is needed.[2]

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