# Childhood Psoriasis Treatment: Evidence Published Over the Last 5 Years

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**Abstract:** Psoriasis is a common skin condition seen in pediatrics. Treatment modalities used to treat psoriasis in children are different from those prevailing in the adult population and require adequate testing in pediatric subjects. This article reviews the published evidence on the different treatment modalities for pediatric psoriasis over the past 5 years.

**Keywords:** Psoriasis, treatment, children.

## INTRODUCTION

Although the true prevalence of psoriasis in the pediatric population is not well established, it is estimated to represent 4% of all dermatoses presenting in patients less than 16 years of age, making it a common pediatric condition [1]. Approximately one third of patients who suffer from psoriasis will begin to develop symptoms within the first two decades of life [2]. The most frequent age of onset during childhood remains elusive, with studies presenting different ranges of disease onset (0 to 4 years [3] vs. 6 to 10 years [4]).

Psoriasis is a chronic, multisystemic, autoimmune disorder, characterized by hyperproliferation of epidermal keratinocytes and inflammation of the epidermis and dermis. Although its pathogenesis remains unclear, it is widely hypothesized to be a complex interaction involving immunologic and environmental factors in a genetically predisposed host. Precipitating factors are more common in childhood than in adult onset psoriasis [2]. Infections (especially group A beta haemolytic streptococcus) [5], drugs [6], and stress [7] have been implicated in both the initiation and exacerbation of early onset psoriasis. These triggers are thought to evoke an inflammatory response which results in subsequent hyperproliferation of keratinocytes. Strong evidence for genetic susceptibility has also been gradually elucidated. Epidemiologic studies have indicated a higher risk of developing psoriasis in those with first degree relatives who are also affected than compared to those without any affected relatives [8]. Twin studies have shown a 75% disease concordance rate in monozygotic twins [8]. Furthermore, up to 9 psoriasis susceptibility loci have been detected by linkage studies as major genetic determinants for early onset psoriasis [9].

Psoriasis in childhood can have different presentations that may evolve over time. In a clinical review of 1262 patients with psoriasis, the most common variants in order of frequency were plaque type, followed by psoriatic diaper rash with dissemination, scalp, anogenital, and guttate types [3]. Pustular and nail psoriasis were not found to be prevalent in this particular study. Psoriatic diaper rash is a clinical variant unique to young children under 2 years of age. It presents with bright red sharply demarcated lesions, involves the inguinal folds, and is often followed with widespread eruptions of erythemato-squamous lesions. Guttate psoriasis is another subtype occurring more often in children than in adults, linked to streptococcal infections [5]. These papular lesions appear abruptly and are usually scattered symmetrically over the trunk, proximal extremities, face, and scalp.

Diagnosis of psoriasis is usually clinical and based on recognition of classic clinical features. Lesions typically consist of well-defined, erythematous papules and plaques of various sizes, associated with silvery scales. These lesions are more clearly demarcated than eczematous patches, are less itchy, and may also have an annular configuration. There are differences in the clinical manifestations of pediatric and adult onset psoriasis. Plaques of psoriasis in children are often smaller, with softer, finer scales than compared to adults. Facial and flexural surface involvement is also more common in children than in adults.

As psoriasis is a chronic disease with periods of remission and exacerbations, treatment can be challenging. Management decisions must take into consideration the type, severity, and sites of psoriasis, in addition to safety concerns and accessibility to treatment. Topical therapies are the first line treatments used in psoriasis and are often sufficient to control the disease. Corticosteroids remain the first line topical agents. However, very high potency steroids should be avoided in children if possible or used sparingly in combination regime with steroid-sparing alternatives, such as coal tar, vitamin D analogues, or retinoids. In cases of refractory, diffuse, or severe forms of psoriasis, more aggressive systemic treatments, such as retinoids, Cyclosporine, and Methotrexate, or ultraviolet light therapy are indicated. Newer, more targeted biologic treatments, specifically tumor necrosis factor alpha [TNF-$\alpha$) inhibitors, are also gaining popularity in the management of refractory psoriasis. Although various therapies are available, there are limited numbers of clinical trials to guide the use of these products in children. The goal of this paper is to review the evidence gathered within the last 5 years for therapies targeted towards the management of psoriasis in the pediatric population.

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## METHODS

A literature search was conducted on Medline for evidence on treatment modalities for pediatric psoriasis published within the last 5 years (from January 2005 to December 2009). The search was conducted with the term "childhood psoriasis," with the following limitations: "randomized controlled trials," "clinical trials," and "treatment". This search strategy produced 28 articles, of which 11 were excluded as they were review articles in nature. Articles that presented data about treatment modalities exclusively on pediatric patients or in which the pediatric patients were analysis separately from adult patients were included in the study. Thus, a final number of 17 articles, all of which fit our inclusion criteria, were included in this review.

Articles were reviewed and classified into five categories: topical treatments, systemic treatments, biologics, UV therapy and combination therapies. Each article was graded on the level of evidence its information provided, as proposed by Harbour *et al.*: 1++ (high quality meta- analyses, systematic reviews of RCTs or RCTs with a very low risk of bias), 1+ (same study types as 1++, that were well conducted and have low risk of bias), 1- (same study types as 1++ with a high risk of bias), 2++ (high quality systematic reviews of case-control or cohort studies or high quality case-control or cohort studies with a very low risk of confounding, bias, or chance and a moderate probability that the relationship is causal), 2+ (same study types as 2++ with a low risk of confounding, bias, or chance and a moderate probability that the relationship is causal), 2- (case-control or cohort studies with a high risk of confounding, bias, or chance and a significant risk that the relationship is not causal), 3 (non-analytic studies: case reports, case series), 4 (expert opinion) [10].

## TOPICAL TREATMENTS

### Corticosteroids

Despite a lack of reliable scientific evidence, corticosteroids remain the first line agents in the topical treatment of psoriasis in all ages. They are highly effective in the treatment of psoriatic lesions, due to their anti-inflammatory and anti-proliferative properties [11]. They range in potency from very weak Class VII agents to extremely potent Class I agents as ranked by the Stoughton-Cornell vasoconstriction classification [12]. Clobetasol is a Class 1 agent (super potent), and it is rarely used to treat psoriasis in pediatric patients.

A phase III, multicenter, randomized, double blind study assessed the efficacy and safety of a class IV topical corticosteroid, clobetasol propionate [13]. Clobetasol 0.05% emulsion formulation (EF) was compared to vehicle applied twice daily for 2 consecutive weeks in participants with mild to moderate plaque type psoriasis. Of the subpopulation of 9 adolescents [12-18 years of age), a moderate proportion of 25% of participants attained treatment success in the clobetasol EF group, compared to 0% in the control group. The most common side effects of this intervention were application site burning or atrophy. Other local side effects, such as the presence of striae, telangiectasias, and acneiform eruptions, as well as systemic adverse effects including adrenal suppression, were not found in this study.

### Steroid Sparing Topical Agents

Vitamin D analogues such as Calcitriol and topical retinoids such as Tazarotene are also alternatives to corticosteroids for treatment of psoriasis, and are frequently used as steroid sparing agents. Calcitriol mediates its effect through the differentiation of keratinocytes and inhibition of their proliferation [14]. The mechanism of tazarotene is through the restoration of normal epidermal differentiation and proliferation, in addition to the reduction of epidermal inflammation [15]. A single-centre, investigator blinded, prospective cohort study from Taiwan compared the efficacy and safety of Calcitriol versus Tazarotene in the treatment of plaque psoriasis [16]. All 23 patients in the study, with a wide age range of 12 to 80 years, had Calcipotriol 0.005% ointment applied twice a day to one side of the body and Tazarotene 0.1% gel applied once in the evening and petrolatum once in the morning to the other side for 12 weeks. One to three target lesions that were similar in anatomic location and degree of severity were followed in each patient. At the end of 12 weeks, there were no clinically significant differences found between the efficacy of Tazarotene and Calcipotriol in the reduction of lesion severity. Upon further analysis, the onset of treatment effect in the Tazarotene treated side was delayed compared to the Calcipotriol side (4 weeks vs. 1 week). However, Tazarotene provided superior maintenance effect at week 16. The side effects of both topical therapies were limited to local cutaneous irritation, with higher rates of these adverse effects associated with Tazarotene treated lesions. In addition to treatment of plaque psoriasis, Tazarotene 0.05% has been implicated in the successful treatment of childhood nail psoriasis [17]. Significant improvement in hyperkeratosis, decrease in nail fragility, and resumption of normal nail growth were observed in a case report, after 8 weeks of application. Similar to the previous study, side effects of the treatment were limited to local cutaneous irritation.

The number of recent publications on the topical treatment of pediatric psoriasis are limited. The three studies highlighted in this review describe safe and effective options in the treatment of mild to moderate plaque and nail psoriasis in the pediatric population. However, all 3 studies had extremely small sample sizes of participants less than 18 years of age, ranging from 1 to 9, and was unspecified in one study. Furthermore, follow up periods of these studies range from 2 to 16 weeks, a time period not extensive enough to draw conclusions regarding long term efficacy and safety of the treatments.

### Systemic Treatments

In children, psoriasis usually follows a benign course and is successfully managed with topical agents [18]. However, in refractory or severe forms of the disease, more aggressive systemic treatments, such as retinoids, cyclosporine, or methotrexate, are required.

### Retinoids

Retinoids, such as acitretin or isotretinoin, are the most commonly used oral medication in the treatment of psoriasis. These compounds possess vitamin A activity and exert their physiologic effects by altering cellular metabolism, epider-

mal differentiation, and apoptosis [19]. Several recent case reports have documented the effectiveness of these agents in the treatment of refractory psoriasis. A 2.5 month infant with a widespread flare of infantile pustular psoriasis responded rapidly to a course of acitretin 10 mg twice a week in combination with daily oral Prednisolone (0.3 mg/kg), clearing the rash within 4 months [20]. Similarly, a 16 year old girl of Saudi origin with a flare of generalized pustular psoriasis was started on Isotretinoin 40 mg/day (0.75 mg/kg/day) after relapsing on methotrexate [21]. The regime successfully controlled her disease. The most important adverse effects with long term (>6 months) use of retinoids are skeletal complications, such as hyperostotic changes, calcification of tendons and ligaments, and premature closure of the epiphysis [22]. This was not observed in either of the two reported case studies. However, close monitoring of growth parameters and yearly radiology skeletal surveys are recommended during the course of retinoid therapy [23]. Another important adverse effect of both isotretinoin and acitretin is the potent teratogenicity of the drugs. Due to concerns regarding this serious side effect, reliable methods of contraception are required in females of child bearing age during the course of treatment, as well as for 4 weeks following treatment discontinuation of isotretinion and for 3 years following discontinuation of acitretin. The rapid clearance time of isotretinoin makes it more preferable for females of childbearing age. Another common adverse effect of retinoids is the elevation of lipids, specifically triglycerides. A transient rise in lipids was observed in the infantile pustular psoriasis case, with levels normalizing within a month of treatment cessation and no detrimental sequelae observed. Other common adverse effects associated with retinoid use in the pediatric population include elevated liver enzymes as well as mucocutaneous effects such as cheilitis, epistaxis, and blepharoconjunctivitis [24].

## Cyclosporin

Cyclosporin is another alternative for the systemic treatment of childhood psoriasis. Its immunosuppressive mechanism is mediated through the inhibition of T lymphocytes and proinflammatory cytokines, specifically Interleukin-2 and Interferon gamma [25]. Its success in the treatment of severe refractory plaque and pustular psoriasis was reported in a case series of 6 children between 11 months to 13 years of age [25]. Marked lesion improvement was observed in 3 of the 6 children after 2 to 3 months of therapy with doses of 2-4 mg/kg/day. These children remained in remission at 1 year follow up. The other 3 children experienced marked improvement with cyclosporine but quickly relapsed when the dosage was tapered. They were subsequently started on a combination of cyclosporin and acitretin, with good responses at 6 months follow up. Well documented serious adverse effects associated with long term cyclosporin use include nephrotoxicity and hypertension. These side effects are dose dependent and in almost all cases are reversible after discontinuation of therapy [26]. None of the patients in the case series experienced renal dysfunction, high blood pressure, or other commonly associated symptoms such as nausea, diarrhea, joint pains, muscle aches, tremors, or headaches throughout the course of treatment (mean of 54 weeks). It can be concluded from these observations that cyclosporine is extremely effective treatment, either as monotherapy or in combination with oral steroids. Provided that patients are monitored for side effects, treatment with cyclosporine can be continued safely for up to 2 years [27].

## Methotrexate

Methotrexate is an antimetabolite folic acid analogue used in the treatment of various malignancies and autoimmune diseases, such as psoriasis. Its mechanism of action is mediated through the competitive inhibition of dihydro folate reductase, resulting in interference of DNA synthesis, giving rise to decreased epidermal and lymphocytic proliferation [28]. Several studies have reported efficacy and limited side effects with the use of methotrexate in the treatment of paediatric psoriasis. Collin *et al.* conducted a retrospective case review of 13 patients aged 3 to 15 years with severe plaque psoriasis, who were treated with methotrexate at a dosing range of 0.1-0.41 mg/kg once weekly for a mean of 71 weeks [29]. Eleven of the patients responded well, with lesion clearance and minimal residual disease. Five of these children required ongoing treatment in order to maintain disease control and another 4 required reintroduction of methotrexate due to relapse. Of the 2 patients who did not respond, one elected to stop treatment after 6 weeks and another was unable to continue due to significantly raised liver enzymes.

Another retrospective case review conducted by Kaur *et al.* analyzed the treatment course of 24 patients from India between the ages of 2.5 to 14 years with refractory plaque psoriasis and generalized pustular psoriasis [28]. Doses of methotrexate given ranged from 0.2 to 0.4 mg/kg once weekly. An excellent response to therapy was objectively measured as more than a 75% decrease from baseline PASI (Psoriasis Activity and Severity Index) scores. Overall, 22 patients achieved excellent responses and the remaining 2 reached modest responses (50 -75% decrease in PASI scores). Mean time for control of disease ranged from 3 to 10 weeks, with remission periods varying from 1.5 to 3 years. Subsequent relapses were managed topically, as none were deemed severe enough to warrant a repeat course of methotrexate. Although extremely efficacious, the side effect profile of this therapy makes it unfavourable in the pediatric age group. The most important consequence is potentially reversible liver fibrosis [30]. Currently there is lack of a specific noninvasive screening or monitoring test to detect the presence and severity of hepatic fibrosis, and unfortunately liver biopsy remains the only reliable diagnostic test. Transiently elevated liver enzymes are another important consequence of methotrexate. Colline *et al.* observed that 9 out of 13 patients experienced transient rises in liver enzymes while on methotrexate; most had very minimal elevations. However, one obese child had extremely disturbed liver function tests (AST = 383, ALT = 516) after 6 weeks of treatment. Subsequent liver biopsy revealed no fibrosis but evidence of fat infiltrates which may point non-alcoholic steatohepatitis (NASH). This underlying metabolic condition was thought to compound the hepatotoxicity of Methotrexate. Given the prevalence of NASH, the therapy should be used with caution in obese children. Bone marrow toxicity is the other serious and potentially life-threatening side effect associated with methotrexate use, and can occur within the first 4 to 6 weeks of treatment [31]. Patients supplemented with folic

acid have increased tolerability and substantially reduced risk of pancytopenia without alteration of efficacy [32]. Other common side effects associated with methotrexate use include stomatitis, nausea, and vomiting [33]. Both Kaur *et al.* and Collin *et al.* reported a large number of patients who experience these mild adverse effects (38% and 46% respectively). These symptoms were easily controlled with either antiemetics, by changing the route of medication administration (from oral to subcutaneous or intramuscular), or by supplementation with folic acid.

The three most commonly used systemic treatments for psoriasis in children, as in adults, are acitretin, cyclosporine, and methotrexate. Randomized controlled trials evaluating the efficacy and safety of these systemic therapies in the pediatric population are lacking. Instead, the evidence is limited to case reports and case series that provide lower levels of evidence for their use. However, the literature does provide a strong consensus regarding the efficacy and safety of all 3 therapies in the treatment of refractory and severe psoriasis, given careful follow up and monitoring of side effects.

## Biologics

Biologic agents were introduced at the end of the 1990's for the treatment of rheumatoid arthritis. These target and block specific immunologic factors and this is why they seemed promising for inflammatory conditions such as psoriasis. In patients with psoriasis, the immune system launches a cytokine response that exaggerates the inflammatory response and leads to the epidermal hyperproliferation and perpetuation of the disease. Biologic agents, such as etanercept, infliximab, adalimumab and TNF-α antagonists, have the potential to put a stop to the inflammatory pathways active in psoriasis.

The evidence published in the last 5 years on the use of biologic agents in pediatric psoriasis, include a case report, two case series and a randomized, double-blinded, placebo-controlled trial which are discussed in detail below.

## Infliximab

The case report described a 3 year old girl that presented generalized pustular psoriasis refractory to systemic treatment (cyclosporine A, acitretin, corticosteroids) with initial positive response to infliximab, and clearance of disease after two weeks of using this medication [26]. The dose used was 75 mg (5m/kg) at weeks 0, 2 and 6 and then every 7 weeks thereafter. Patient remained on remission for 10 months, and at this time presented thick scalp scales and was thus started on metotrexate. She presented a flare-up of her condition after a year of treatment with infliximab, and at this time infliximab was discontinued and she was restarted on cyclosporine A, corticosteroids and due to non-reponse, acitretin was also added. After three months she continued presenting pustular eruptions and etanercept was initiated (0.4 mg/kg) twice a week for 2 months and then once a week. The patient slowly improved over a 4 week period and remained without pustular eruptions 6 months after. The patient's response to biologics was faster with infliximab, and nail changes also improved with this agent; the response to etanercept was slower, nails did not improve as much, but no transient flares were seen.

## Etanercept

The second publication reports a prospective case series of patients that used etanercept for severe childhood psoriasis. They present 4 cases, an 11 year old with pustular erythrodermic generalized psoriasis, a 6 year old and a 15 year old both with plaque psoriasis and a 15 year old with severe plaque palmoplantar psoriasis [34]. Patients were treated with 0.4 mg/kg of etanercept twice weekly, 2 had complete remission after 12 weeks of treatment, ant the other two patients achieved a 50% improvement of PASI score at week 12. Continued treatment resulted in a 75% improvement by week 24. Treatment was well tolerated and no adverse events were reported. In one patient treatment was stopped after 48 weeks, and he relapsed after two months, he was re-treated and responded, presenting a PASI of 0 12 weeks after resuming treatment.

The third publication presents a retrospective case series of patients that used etanercept for severe, generalized, recalcitrant psoriasis (7 patients with plaque psoriasis, 1 guttate, and one pustular, psoriatic arthritis) from two different pediatric dermatology centers [35]. They used subcutaneous injections at 25 mg, or 0.4 mg/kg/dose, biweekly, or 50 mg once per week. Patients' ages ranged between 8 and 18 years, with a mean of 13.5 years. Four patients were initially treated only with etanercept, one stopped topical medications after starting etanercept and the remaining used concomitant therapies while on etanercept. Three patients had clearance of their psoriasis after 3 to 6 months of treatment and stopped the medications, but re-flared and had to restart it. Overall, 2 patients had equivocal/insignificant effect, and the remaining patients had marked and sustained improvement (based on clinical records). The most common adverse effects reported were local skin irritation and ecchymosis at injection site.

The last publication on biologics for pediatric psoriasis presents a randomized, double-blinded, placebo-controlled, phase 3 study that assessed the efficacy and safety of etanercept in pediatric patients with moderate-to-severe plaque psoriasis, and provides the best evidence in this treatment category [36]. Subcutaneous injections given once-weekly of etanercept at a dose of 0.8 mg/kg were compared to placebo. At week 12 more patients that received etanercept (60/106 vs 12/105) achieved a PASI 75 ($P<0.001$), and a significant difference was seen as early as week 4.

Since biologics are relatively new drugs, most of the concerns regarding their use are due to their long term safety. The possible side-effects of these medications are concerning, particularly in pediatric patients were their used has been even more limited. A major concern is regarding the possibility of lymphomas developing secondary to their use.

## UV Therapy

Another modality for treating psoriasis is light or ultraviolet (UV) treatment. Three studies were identified looking at UV therapy for pediatric patients.

The first study looked at the use of narrow-band UV-B phototherapy in 20 patients with psoriasis that had more than 20% of body surface area involved (18 had plaque psoriasis and 2 guttate). The NB UV-B therapy was started at a dose

**Summary Table**

| | Study | N | Intervention | Conclusion | Level of Evidence |
|---|---|---|---|---|---|
| **Topical** | Kimball *et al.* | 497 | Clobetasol 0.05% vs. control | Clobetasol found to be more effective than control. Side effects limited to local paresthesia and atrophy. | 1- |
| | Tzung *et al.* | 23 | Calcipotriol 0.005% vs. Tazarotene 0.1% | Similar efficacy between the 2 treatments. Calcipotriol provided faster onset of action but Tazarotene offered better maintenance effects. Local cutaneous irritation was significantly greater in the Tazarotene group. | 2- |
| | Diluvio *et al.* | 1 | Tazarotene 0.05% | Improvement of nail psoriasis with no relapse. Side effects limited to local skin irritation. | 3 |
| **Systemic** | Kaur *et al.* | 24 | Methotrexate 0.1-0.41 mg/kg once weekly | Excellent response to therapy in 92% of patients. Side effects included nausea, vomiting, loss of appetite in 38% of patients. | 3 |
| | Collin *et al.* | 13 | Methotrexate 0.1-0.41 mg/kg once weekly | 85% of patients responded well with lesion clearance. 69% experience transient elevations in liver enzymes. 46% experience mild GI side effects. | 3 |
| | Pereira *et al.* | 6 | Cyclosporin 2-4 mg/kg/day | Marked lesion improvement was observed in 50% of patients who remained in remission at 1 year follow up. No systemic side effects observed. | 3 |
| | Ergin *et al.* | 1 | Acitretin 0.5 mg/kg/day | Cleared infantile pustular psoriasis within 4 months with relapse after a remission period of 15 months. | 3 |
| | Al-Shobaili *et al.* | 1 | Isotretinoin 0.75 mg/kg/day | Cleared generalized pustular psoriasis after 2 weeks. No reported side effects. | 3 |
| **Biologics** | Pereira *et al.* | 1 | Infliximab 5mg/kg at weeks 0, 2, 6, and every 7 weeks after that Etanercept 0.4mg/kg/day twice weekly | Patient with generalized pustular psoriasis that was refractory to cyclosporine A, acitretin and steroids responded well to biologics. | 3 |
| | Papoutsaki *et al.* | 4 | Etanercept 0.4 mg/kg twice weekly | Etanercept may be efficacious and well tolerated for severe forms of childhood psoriasis. | 3 |
| | Hawrot *et al.* | 9 | Etanercept 25 mg or 0.4mg/kg/dose biweekly or 50 mg once per week | Results ranged from equivocal/insignificant effect in 2 patients to marked and sustained in the remaining 7 | 3 |
| | Paller *et al.* | 211 | Etanercept 0.8 mg/kg/wk for 12 wk vs placebo followed by 24 wk of Etanercept at the same dose (open-label) At week 36, 138 patients were randomized to placebo or etanercept for 12 weeks | Etanercept significantly reduced disease severity in children and adolescents with moderate-to-severe plaque psoriasis. Four serious adverse events occurred in the open label part of the study: an ovarian cyst removal, gastroenteritis, and gastroenteritis-related dehydration, pneumonia. Longer term data is needed to fully assess the safety profile of Etanercept. | 1+ |
| **UV therapy** | Kumar *et al.* (2007) | 20 (2 withdrew due to inability to attend sessions) | Narrow band UVB twice a week starting at 50mJ with increments of 10% per session in the absence of erythema | In 12 patients PASI decreased by 90% or more, in 3 patients had 70-90% improvement of PASI scores, 1 had 50-70% improvement of PASI and in 2 PASI improved less than 50%. Side effects: 2 patients presented erythema. NB UVB is an effective and safe treatment modality for childhood psoriasis. | 3 |

**Table Contd…**

| | Study | N | Intervention | Conclusion | Level of Evidence |
|---|---|---|---|---|---|
| | Ersoy-Evans *et al.* | 68 | UVB (0.1 J/cm2, increased by 0.01-0.03 J/cm2 per treatment), narrow band UVB (70% of the minimal erythema dose, 20% dose increases with each session), PUVA (0.5 J/cm2 with increments of 0.5 J/cm2). All given 3 times/week and then 2 times/week when patients responded. | Response rate in psoriasis patients was 83.3% with PUVA, 93.3% with UVB and 92.9% with narrow-band UVB. Phototherapy is a well-tolerated treatment for childhood dermatoses, and is especially efficacious in psoriasis. | 3 |
| | Kumar *et al.* (2008) | 18 | NB UVB 50 mJ/cm2 with 10% increments per session, twice a week. | The use of mineral oil prior to irradiation enhances the therapeutic efficacy of narrow-band UVB. | 2- |
| **Combined Therapies** | Borska *et al.* | 26 | Crude coal tar ointment + UVA and UVB | Significant clinical amelioration of disease activity was found. The study neglected to comment on adverse effects. | 3 |
| | Kim *et al.* | 1 | Induction: Cyclosporine A 1 mg/kg/day<br>Maintenance: NB UVB + Acitretin 0.3 mg/kg/day | Improvement of disease after 2 months. Side effect limited to slight transient elevation of liver enzyme levels, attributed to Cyclosporine induction. | 3 |

of 50 mJ twice a week (on non-consecutive dates) and was incremented by 10% at each session if there was no trace of erythema. PASI scores were performed at baseline, 4, 8 and 12 weeks of treatment. Two patients withdrew from the trial due to inability to attend UV-B sessions. The cumulative clearance dose of UV-B had a mean of 4286.5 +/- 1522.1 mJ/cm2 and the mean highest dose per treatment was 329.5 +/- 90.3 mJ/cm2. The number of treatments that were required for clearance ranged from 17 to 30 (mean 24.2 +/- 3.7). By the end of week 12, 12 patients had excellent response (90% or more reduction in the PASI score), 3 had a good response (70-90% improvement of PASI), 1 had a moderate response (50-70% improvement of PASI and 2 had no response (PASI improved less than 50%). Only 1 patient relapsed after 5 months and required NB UV-B therapy again, the remaining patients did not present significant relapses in a 6-month follow-up period. The only adverse effects reported were mild erythema in 2 patients. Authors concluded that NB UV-B is an effective and safe treatment modality for childhood psoriasis, and suggest that it should be considered before more toxic systemic therapies.

The second publication is a retrospective chart review that reported on the efficacy of phototherapy in childhood dermatoses on 113 patients 17 years of age or younger, of whom 68 patients were diagnosed with psoriasis. Psoriasis represented the most common indication for phototherapy, and the median age of psoriatic patients treated with phototherapy was 12 years (range 5-17 years). The modalities of phototherapy used in these patients were: UVB phototherapy (n=30, 44.1%), narrow-band UVB (n=28, 41.2%), PUVA (n=7, 10.3%), topical meladinine and UVA (n=2, 2.9%) and local UVA (n=1, 1.5%). Most of the patients treated with phototherapy had guttate-type psoriasis (n= 59, 88.8%) followed by plaque psoriasis (n=6, 8.8%). Response, defined as more than 75% improvement in skin lesions that led to a decrease in the frequency of treatments, was achieved in 92.9% of patients treated with narrow band UV-B, 83.3% of patients treated with PUVA and 93.3% of patients treated with UVB. The mean number of treatments required to achieve response with the different modalities was not statistically significant (mean number of treatments for PUVA was 28, for UVB 18.5 and for narrow band UVB 16).

The last publication on phototherapy treatment in psoriasis presents a prospective, single-blinded, controlled study trying to determine if the use of mineral oil pre-irradiation with NB-UVB enhances its effect. Twenty children ages 5 to 14 were enrolled, but only 18 completed the study. Patients had widespread, symmetrical psoriasis involving more than 20% body surface area and had type IV skin. Mineral oil was applied to half of the body 5 minutes before treatment that consisted of twice weekly NB-UVB at a starting dose of 50 mJ/cm2 and incrementing by 10% with each session. The same physician evaluated all patients, and he was blinded as to which side had received the mineral oil. Parameters evaluated were erythema, scaling and induration (as in the modified PASI score and were graded 0 to 4), as well as area of involvement and modified PASI score. The mean cumulative dose for clearance, the maximum NB UVB dose for clearance and the mean number of exposures required for clearance on the mineral oil pretreated side were significantly less than over the non-pretreated side ($p<0.001$, $p<0.001$ and $p<0.05$ respectively). The conclusions of this study are that the use of mineral oil is an optimal emollient for preirradiation use with NB UVB as it enhances the efficacy and results in shorter treatment periods and lower cumulative doses.

### Combination Therapies

For enhanced therapeutic effect and reduced toxicity of each individual agent, various combinations of topical, systemic, and photo therapies may be used. Caution is advised, as interactions may cause toxicities to accumulate. Thus individual agents must be carefully considered before concurrent use.

The Goerckerman regime, often used as first line therapy of psoriasis in the Czech Republic, consists of concurrent topical application of crude coal tar ointment with daily UV-A and UV-B exposure (1 to 15 minutes in duration). Borska *et al*. prospectively followed 26 pediatric patients age 8 to 17 years who underwent this regime in order to assess its efficacy [37]. After an average duration of 19 days of treatment, mean PASI scores in the pediatric cohort declined from 26.2 to 5.08 ($p < 0.001$), indicating significant clinical amelioration of disease activity. Though efficacious, the study neglected to comment on adverse effects. Furthermore, with no control group to assess the individual efficacy of each treatment, it is difficult to measure the true synergistic effect of the Goerckerman regime.

Another approach to combination therapy is the division of treatment into an induction and a maintenance phase. This method proved to be effective in the management of severe generalized pustular psoriasis in an 8 year old Korean boy [38]. Low dose Cyclosporine A at 1 mg/kg/ day was given orally for two months, until toxic symptoms of the disease had disappeared. After tapering of Cyclosporine, focal papules and pustules began to re-emerge. In order to avoid the side effects of long term Cyclosporine use, once weekly narrowband UV-B (NBUVB) phototherapy in adjunction to Acitretin 0.3 mg/kg/day was chosen as maintenance therapy. At 2 months follow up, the disease was still in remission. Except for a slight transient elevation of liver enzyme levels with Cyclosporine induction, no other adverse effects were reported.

The literature on combination therapies for psoriasis in the pediatric population is extremely scarce. Reports are often limited to case studies and case reviews, with no adequate control groups for comparison. Thus, the true synergistic effects of reported adjunct therapies are unclear. However, if long-term treatment is anticipated, rotation of individual agents after a period of time does result in reduced overall cumulative dose and side effects of each agent [39].

## CONCLUSIONS

Despite the fact that psoriasis in children is a common dermatologic condition, properly designed studies regarding its treatment are lacking. Commonly used medications lack scientific evidence showing their efficacy, and newer treatments do not have long-term post-market surveillance data of their safety. There is still a need to balance disease control with short and long term safety in this prevalent condition, and to carry out studies with higher levels of evidence to support treatment modalities.

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