Update on Pediatric Psoriasis, Part 2: Therapeutic Management

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Pediatric psoriasis is an autoimmune diathesis with a complex immunologic basis. It is associated with extensive psychological morbidity and should be treated rapidly and effectively to limit psychologic effects on children. The most common trigger in childhood is upper respiratory tract infection. Once disease has occurred, treatment is based on severity and presence of joint involvement. Topical therapies include corticosteroids and calcipotriene. UV light, systemic retinoids, and cyclosporine remit cutaneous psoriatic lesions. Methotrexate sodium and etanercept benefit both skin and joint manifestations of psoriasis. Concern for psychological symptoms and psychological growth is needed in treating pediatric patients with psoriasis vulgaris.

Psoriasis vulgaris of childhood is a complex immunologic disease. Many new therapies have become available for the treatment of pediatric psoriasis in the last 10 years. Topical therapy remains the first-line treatment of skin-limited disease in children. These agents can be used with a host of oral antibiotics, when indicated. In more severe cases and for chronic illness, systemic therapy and phototherapy are added to help induce improvement and ideally remission. Regardless of the extent of body surface involvement, psoriasis can have negative psychologic and quality-of-life (QOL) effects. Systemic therapies or phototherapy should be considered if lesions are refractory to topical therapies, if the disease involves a substantial body surface area (BSA), or if the patient shows evidence of psoriatic arthritis or reduced QOL. A treatment algorithm for pediatric psoriasis is shown in the Figure.

Topical Therapy
Topical therapy for pediatric psoriasis starts with exfoliants including urea, salicylic acid, and α-hydroxy acids, all of which remove superficial hyperkeratosis, allowing secondary penetration of medications. Coal tar is beneficial, especially when combined with UV light in the Goeckerman treatment. Caution in usage is advised due to reported genomic alterations, including chromosomal aberrations in peripheral blood lymphocytes. There are no topical therapies that are specifically approved by the US Food and Drug Administration (FDA) for the treatment of psoriasis in young children; however, the English-language literature includes many reports of successful improvement in pediatric psoriasis with off-label usage of topical agents. Formulations and strengths should be determined based on patient age, psoriasis global severity scores such as the psoriasis area and severity index (PASI), and impairment of QOL.

Anthralin cream 1%, or dithranol, can be used for localized areas of psoriasis. Side effects include staining of hair and clothing as well as irritation. A head-to-head study of dithranol and calcipotriol applied topically showed that these agents may have similar efficacy. Choice of topical corticosteroids for pediatric psoriasis is similar to therapy for lichenified atopic dermatitis. The head, neck, and intertriginous areas are treated with weaker agents (classes 5–7), while the scalp and extremities generally are treated with mid-potency topical corticosteroids (classes 2–4). Class 1 corticosteroid agents work rapidly in flattening psoriatic lesions but are likely to cause atrophy of the skin, striae, and hypothalamic-pituitary-adrenal...
Diagnose psoriasis

Small BSA affected

Adjunctive Therapies
Emollients/keratolytics
Omega-3 fatty acids (oral)

Evidence of streptococcal infection or rapid-onset cutaneous disease with pharyngitis

Larger BSA affected: moderate to severe disruption in quality of life

Oral antibiotic therapy in addition to topical agents; tonsillectomy in recurrent streptococcal pharyngitis–induced flares

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Topical Agents
Tar (can be combined with UV light therapy)
Anthrakin
Corticosteroids once or twice daily (classes 1–4, body and scalp; classes 5–7, face and intertriginous areas)
Corticosteroids/calciopipriene (each one to be applied once daily)
Calcipipriene or calcitriol once or twice daily
Calcineurin inhibitors twice daily (especially for face and intertriginous areas; for patients aged ≥2 years)

Screening: absence of evidence of prior TB or HBV infection; prior malignancy/lymphoma

Screening examinations: CBC, liver function tests, cholesterol, triglyceride, pregnancy test, blood pressure, urinalysis

Presence of TB, HBV, cancer risk

Biologic Therapies
Etanercept (subcutaneous): 0.8 mg/kg weekly; maximum dosage, 50 mg weekly
Adalimumab (subcutaneous): 40–160 mg loading dosage; 40 mg alternate weekly (dosing based on Crohn disease)
Infliximab (intravenous): 3.3–5 mg/kg at weeks 0, 2, and 6, and then maintenance every 8 weeks

Topical agents (see box to left)
Phototherapy
Topical PUVA
Narrowband UVB

Rotational Therapy
(6–12 months alternating)
Methotrexate sodium: 0.2–0.7 mg/kg per week
Cyclosporin A: 3–5 mg/kg daily
Acitretin: 0.5–1 mg/kg daily

Treatment algorithm for pediatric psoriasis. BSA indicates body surface area; TB, tuberculosis; HBV, hepatitis B virus; CBC, complete blood cell count; PUVA, psoralen plus UVA.
axis suppression with extended usage. One class 1 agent, clobetasol propionate emulsion aerosol foam 0.05%, has been approved for steroid-responsive diseases in children 12 years and older for up to 2 weeks.\textsuperscript{10} Halobetasol also has been tested in pediatric psoriasis (it is not approved in children).\textsuperscript{14} These agents are reserved for short therapy (<2 weeks) of thick stubborn lesions. Clobetasol and halobetasol can be quite effective for usage in psoriatic lesions in adolescents but can run a risk for atrophy due to class 1 corticosteroid status.\textsuperscript{8,10,14} All topical corticosteroids, including products from classes 2 to 7, run a risk for local atrophy and systemic absorption; systemic absorption is more likely when used on larger BSAs. Vitamin D analogues, calcipotriene\textsuperscript{11} and calcitriol,\textsuperscript{9} can thin and clear psoriatic lesions in children. These agents may cause cutaneous erythema or local irritation. Systemic absorption is thought to potentially cause symptoms of hypervitaminosis D, including alterations in calcium levels; however, the risk is small for limited BSA application. Topical calcineurin inhibitors (ie, tacrolimus ointment 0.03%,\textsuperscript{15} pimecrolimus cream 1%\textsuperscript{16}) applied twice daily also can be beneficial for pediatric psoriasis. As these agents do not carry a risk for atrophy, they can be applied to areas of skin at high risk for atrophy, including the face, neck, axillae, groin, and inner thighs. Usage is off label for pediatric psoriasis. Treatment of atopic dermatitis with calcineurin inhibitors is not recommended by the FDA for children younger than 2 years. Topical calcineurin inhibitors bear a black-box warning regarding theoretical skin cancer and lymphoma risks, and combination with UV light is routinely avoided.

**Phototherapy**

Phototherapy is a safe and effective treatment option for children old enough to stand still in a phototherapy booth, particularly in teenagers with extensive disease. A variety of forms of phototherapy can be used to treat pediatric psoriasis, including narrow-band UVB, psoralen plus UVA, and broadband UVB. Delivery systems include hand/foot units, generalized phototherapy booths, and excimer laser systems. Topical psoralsens are preferable to oral psoralsens because of the difficulty wearing protective eyewear for 24 hours after oral psoralsens. Psoralsen plus UVA has been associated with long-term carcinogenicity in adult patients with psoriasis; therefore, narrow-band UVB is likely safer in children.\textsuperscript{17-19} Treatment is performed twice weekly accompanied by protective eyewear and generally requires a few months for clearance and maintenance therapy to prevent future flare-ups. Ocular screening and periodic reevaluation are required for oral psoralsens plus UVA therapy.

**Systemic Agents**

Indications for systemic agent usage in pediatric psoriasis include severe psoriasis (ie, extensive BSA, intractable symptoms), disabling psychological ramifications, and psoriatic arthritis. All systemic agents available for pediatric psoriasis have side effects. Consequently, cyclic usage of 6-month courses of agents is advisable. Longer usage periods have been observed to be safe in rheumatoid arthritis patients using etanercept; however, usage beyond 1 year has not been well-assessed in patients with pediatric psoriasis. Of the systemic therapies, oral antibiotics have the best safety profile in early disease due to their superior side-effect profile.\textsuperscript{1,20-22}

**Oral Antibiotics**—Oral antibiotics have been described to be useful in pediatric psoriasis.\textsuperscript{20-22} Benefits are best noted in the setting of rapid-onset cutaneous disease associated with positive oral pharyngeal cultures, presence of perianal streptococcal disease, pustular psoriasis,\textsuperscript{23} or in psoriasis guttata of childhood. Usage of oral antibiotics has demonstrated mixed results.\textsuperscript{22} The best reported results with oral antibiotic usage were noted in adult patients placed on cyclic usage of azithromycin 500 mg for 4 days out of every 2 weeks for 48 weeks.\textsuperscript{21} Tonsillectomy may be performed in the setting of recurrent streptococcal pharyngitis-induced psoriatic flares.\textsuperscript{21}

**Methotrexate Sodium**—Systemic therapies are most effective in improving QOL for children with chronic and severe psoriasis. Methotrexate sodium is the original therapy available for extensive psoriasis. Collin et al\textsuperscript{24} and Kaur et al\textsuperscript{25} have reviewed case series of children treated with methotrexate sodium for psoriasis. The treatment regimens described are methotrexate sodium dosed at 0.2 to 0.7 mg/kg per week, with frequent achievement of PASI 75 (>75% improvement). Although monitoring complete blood cell counts and liver function tests are required, liver function alteration rarely is observed.\textsuperscript{24-26} Risk factors include obesity and fatty liver changes. Unlike cyclosporine, methotrexate sodium can clear psoriatic arthritis as well as skin disease.\textsuperscript{26} Therapy is started with a small dosage followed by escalating dosages while sequentially monitoring laboratory test results.\textsuperscript{24} Folic acid supplementation protects against pancytopenia, microcytic anemia, and liver enzyme alterations.\textsuperscript{27}

**Cyclosporin A**—Cyclosporin A is a systemic immunosuppressant originally developed to prevent allograft rejection. In dosages of 3 to 5 mg/kg daily, cyclosporine has been shown to reduce skin-limited pediatric psoriasis. Side effects include altered renal function including high blood pressure and increased serum urea nitrogen and creatinine levels. Close monitoring including serum urea nitrogen and creatinine levels as well as blood pressure is required. Although there have been reported risks for malignancy and lymphoproliferative
Biologic Therapies
The injectable drugs etanercept (subcutaneous), adalimumab (subcutaneous), and infliximab (intravenous) can be used in pediatric psoriasis but are not FDA approved for this indication. Tumor necrosis factor α–inhibitor therapies have been used for more than a decade for pediatric autoimmune diseases including rheumatoid arthritis,30 tumor necrosis factor receptor 1–associated periodic syndrome without fever,31 juvenile idiopathic arthritis,32 and Crohn disease.5 Juvenile rheumatoid arthritis patients have the longest usage history with tumor necrosis factor α inhibitors, with up to 8 years of published safety and efficacy data. In a small case series, long-term usage did not seem to increase side effects for children with rheumatoid arthritis.33 An American College of Rheumatology pediatric score reduction of 70% was achieved by all 11 children treated for 8 years and 61% (28/46) of all children treated long term, with no reported cases of tuberculosis, opportunistic infections, malignancies, lymphomas, lupus, demyelinating disorders, or death.30 Long-term improvements on bony disease in arthritis of childhood have been demonstrated with etanercept.33

Anecdotal data have described efficacy of etanercept for pediatric psoriasis.34 Paller et al4 described the results of a phase 2 clinical trial of etanercept in 211 pediatric psoriasis patients aged 4 to 17 years. The study consisted of a 12-week double-blind treatment phase with a 24-week open-label phase. The 12-week data demonstrated a statistically higher PASI 75 and PASI 90 (75% and 90% clearance, respectively) for etanercept-treated children versus placebo. Psoriasis area and severity index 75 was noted in 57% of etanercept-treated pediatric psoriasis patients versus 11% of placebo-treated participants (P<.001) but was lost in 26 of 69 children assigned to placebo on weeks 36 to 48. Four serious adverse events including 3 serious infections (gastroenteritis requiring hospitalization and basilar pneumonia) and an ovarian cyst occurred in participants treated with open-label etanercept; all resolved without sequelae. No deaths, episodes of demyelination, reactivation of hepatitis or tuberculosis, or malignancies occurred. Three patients had transient elevations of hemoglobin levels.4 Two reports of infliximab clearing pediatric psoriasis have appeared in the literature; treatment with oral methotrexate sodium and mycophenolate mofetil had failed in one case and treatment with etanercept failed in another case.6

Natural Supplements
Guardians of children with psoriasis often ask the question “What dietary changes or natural supplements can I give my child to improve his/her skin disease?”2 Although natural supplements or dietary alterations are not curative of psoriasis, disease severity may be reduced with usage of supplements. Fish oil, which contains omega-3 fatty acids, and omega-3 fatty acid supplements often are taken for psoriasis. Inuit populations that eat a diet rich in omega-3 fatty acids/fatty fish have a lower incidence of psoriasis, supporting usage in patients with psoriasis. Both oral and intravenous supplementation have been described for omega-3 fatty acids and the less effective omega-6 fatty acids. These agents may work through alterations in production of arachidonic and docosapentaenoic acids.36 Eating 4 to 6 meals of fish per week can mimic supplementation in reduction of psoriasis.37 One anecdotal report has been published demonstrating that indigo naturalis, a traditional Chinese medicine, helps to clear pediatric psoriasis with 8 weeks’ usage.38

Conclusion
Recent advances in therapeutics for psoriasis have been applied to the pediatric psoriasis population with good results in disease reduction and consequent improvements in QOL. Further data on long-term usage of systemic agents and biologic therapies in children with psoriasis remain to be published.

REFERENCES