

## Childhood psoriasis

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### ABSTRACT

Psoriasis is a common dermatosis in children with about one third of all patients having onset of disease in the first or second decade of life. A chronic disfiguring skin disease, such as psoriasis, in childhood is likely to have profound emotional and psychological effects, and hence requires special attention. Psoriasis in children has been reported to differ from that among adults being more frequently pruritic; plaque lesions are relatively thinner, softer, and less scaly; face and flexural involvement is common and guttate type is the characteristic presentation. Whether onset in childhood predicts a more severe form of psoriasis is a matter of controversy, it may cause significant morbidity particularly if it keeps relapsing. Most children have mild form of psoriasis which can be generally treated effectively with topical agents such as emollients, coal tar, corticosteroids, dithranol, calcipotriol etc. according to age and the sites affected. Narrow band UVB is the preferred form of phototherapy in children for moderate to severe disease or in patients not responding to topical therapy alone. Systemic therapies are reserved for more severe and extensive cases that cannot be controlled with topical treatment and/or phototherapy such as severe plaque type, unstable forms like erythrodermic and generalized pustular psoriasis and psoriatic arthritis. There are no controlled trials of systemic therapies in this age group, most experience being with retinoids and methotrexate with favorable results. Cyclosporine can be used as a short-term intermittent crisis management drug. There is an early promising experience with the use of biologics (etanercept and infliximab) in childhood psoriasis. Systemic treatments as well as phototherapy have limited use in children due to cumulative dose effects of drugs, low acceptance, and risk of gonadal toxicity. More evidence-based data is needed about the effectiveness and long-term safety of topical, phototherapy and systemic therapies in children.

**Key words:** Children, clinical features, epidemiology, India, treatment, psoriasis

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### INTRODUCTION

Psoriasis is a common chronic inflammatory skin disease with a strong genetic basis, characterized by complex alteration in epidermal proliferation and differentiation. Childhood psoriasis is a well-recognized entity, but its true prevalence is not known. Psoriasis can be a life-altering disease with a potentially profound impact on physical, emotional and social functioning and overall quality of life in children. It is aptly said that children are not simply small adults and that is true for childhood psoriasis as compared to psoriasis in adults. The childhood psoriasis differs in epidemiology, clinical features, treatment options, and long-term clinical and psychological outcome.<sup>[1]</sup>

### EPIDEMIOLOGY

Psoriasis is a frequent condition in children, but only limited epidemiologic data are available. Various published large series have reported that of all psoriasis patients, 20 – 35% have onset of their disease before the age of 20 years.<sup>[2,3]</sup> In a study of 419 patients of childhood psoriasis from North India, it constituted 0.3% of the all dermatology outpatients and 12.5% of the total psoriasis patients at a tertiary care hospital.<sup>[4]</sup> Psoriasis comprised 1.4% of all pediatric dermatoses seen in patients less than 14 years of age at a referral hospital in South India.<sup>[5]</sup> In an epidemiological study of various dermatoses in school children aged 6-14 years from North India, the point prevalence of psoriasis was found to be 0.02%.<sup>[6]</sup>

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Psoriasis was the underlying etiology in 15% of all cases of erythroderma in children (less than 12 years of age) from Delhi, India.<sup>[7]</sup>

The peak age of onset in childhood psoriasis varied in different studies. In surveys from India and Denmark, most patients developed first symptoms at the ages of 6 to 10 years,<sup>[4,8]</sup> whereas other studies from the Middle East and Australia reported a peak of onset at the ages of up to 4 years.<sup>[9,10]</sup> Studies from the Denmark and Middle East have shown a female preponderance,<sup>[8,9]</sup> but reports from India and Australia have documented equal sex predisposition.<sup>[4,10,11]</sup>

According to the bimodal age of onset, two types of psoriasis have been distinguished. Type I (onset 15–40 years) accounts for the majority of cases (>75%) and shows a high degree of familial aggregation and strong association with HLA Cw6. Correspondingly, type II begins after the age of 40 years and tends to be less severe.

The genetic basis of the disease has been convincingly established by epidemiologic and twin study data. A number of studies indicate toward the increased risk of developing psoriasis if relatives are affected<sup>[12]</sup> but data regarding its familial aggregation are inconsistent.<sup>[10,13]</sup> The inheritance pattern of psoriasis remains unclear. Familial prevalence is observed to be greater in childhood psoriasis than in adult-onset psoriasis. Compared with 37% in adult-onset patients, 49% of pediatric-onset patients had first-degree family members affected with psoriasis.<sup>[13]</sup> Some studies have reported familial incidence in childhood cases of psoriasis as high as 89%.<sup>[14]</sup> The relatively low familial incidence of psoriasis of about 4.5 - 9.8% among Indian patients could be explained by the ignorance of family members about the existence of the disease, an attempt to hide information because of social reasons or the actual absence of the disease at the time of enquiry.<sup>[4,11]</sup> Twin studies yielded a concordance in monozygotic twins between 35 and 75%.<sup>[12]</sup> Although about 20 genetic loci associated with psoriasis have been reported from linkage-based studies, only 1 of these linkage-based loci, PSORS1, that includes the HLA-C gene on chromosome 6p21, has been universally confirmed and is considered to confer susceptibility to early-onset psoriasis.<sup>[15,16]</sup>

#### **CLINICAL FEATURES OF PSORIASIS IN CHILDREN**

Childhood psoriasis has been reported to differ from

psoriasis in adults in that it is more frequently pruritic, preponderance in girls, and the lesions are relatively thinner, softer, and less scaly. Similar to adults, plaque type is the most common form of disease but certain clinical variants are rare in children, such as erythroderma, arthropathy, and localized and generalized pustular psoriasis.<sup>[1-6]</sup> In general, psoriasis in children is more frequently precipitated by infections and physical and psychological trauma than it is in adults.<sup>[1,4,5,17]</sup> The frequency of remissions has also been found to be greater in pediatric-onset psoriasis than in adult-onset disease.<sup>[13]</sup> Psoriasis in infants often starts in the napkin area but a definitive diagnosis at this stage may be difficult. Flexural psoriasis of the genital and periumbilical regions is common and may be the only manifestation of disease;<sup>[17]</sup> however, such involvement is rare in infantile psoriasis in India.<sup>[4]</sup> This could be explained by the fact that, in India, western-type diapers (which are thick and of an occlusive nature because they are meant to soak and retain urine and secretions) are not used by most parents for their children. The increased bacterial and fungal growth levels due to occlusion may initiate the psoriatic lesions in predisposed individuals.<sup>[18]</sup> Therefore, this could explain the higher percentage of diaper region involvement in the Australian study.<sup>[10]</sup>

Typically, childhood psoriasis manifests as acute guttate psoriasis.<sup>[17]</sup> Reports from India suggest that children tend to manifest the established plaque type of disease more often, rather than the transient guttate form.<sup>[4,11]</sup>

Facial involvement in children is a frequent observation in majority of the reports varying from 18 to 46%.<sup>[8,19]</sup> However, this figure is as low as 4.71% from India where children in the tropical environment are exposed to the ultraviolet (UV) rays of the sun all the time, and hence have less frequent involvement of sun-exposed sites.<sup>[4]</sup> This observation in children with psoriasis is also made from countries like Middle East<sup>[9]</sup> and Australia<sup>[10]</sup> where there is a lot of sunshine. Pityriasis amiantacea often represents scalp psoriasis in children.<sup>[17]</sup>

Pustular psoriasis is rare in children. Generalized pustular psoriasis is slightly more common in boys than girls, in contrast with nonpustular psoriasis in childhood and pustular psoriasis in adults. The von Zumbusch pustular psoriasis is more common in infancy whereas annular forms appear later and mixed patterns

also occur. Although localized pustular psoriasis is extremely rare in children, parakeratosis pustulosa is often a manifestation of psoriasis. Psoriatic arthritis is relatively uncommon. Nail involvement is observed in one-third of patients and palms and soles involvement is uncommon.<sup>[1,4,9,11]</sup> In a study from India, the soles were the most frequent site of onset after the legs and scalp in 12.8% of children, which is in sharp contrast with a previous study from Australia where plantar involvement was reported in only 4%.<sup>[10]</sup> This may be due to the habit of walking barefoot or wearing open sandals in India, leading to a degree of koebnerization at these friction-prone sites,<sup>[20]</sup> especially in children who are generally more active.

Mucosal involvement has been exceptional rare in Indian children as compared to reports from other parts of world reporting figure of up to 7% in childhood psoriasis.<sup>[9]</sup> Similar to observations from other countries,<sup>[9]</sup> disease is mild in majority of Indian children. There seems to be no positive correlation between the early age of onset, severity of involvement, and family history of disease in Indian children with psoriasis.<sup>[4,11]</sup>

## MANAGEMENT

### *General principles*

Fortunately, the disease is mild in majority of cases and can be managed adequately with the topical medications. The true challenge exists in treating the subset of children who present with severe, rapidly evolving, debilitating, and frequently relapsing psoriasis. The objective of the treatment of psoriasis in children is to improve the physical and psychological symptoms, minimizing the effect of disease on psychosocial development and limiting the adverse effects of drugs on future health. Therapeutic modality should consider the patient's and the parents' attitude toward the disease; the type, severity, extent, and sites of psoriasis; as well as safety concerns and accessibility of treatment.<sup>[17,21,22]</sup> Complete clearance of disease may be unrealistic in all patients and relapse is frequent, thereby emphasizing the need of control versus cure as setting a realistic expectation for treatment. Randomized controlled clinical trials involving children under the age of 12 years, suffering from psoriasis have been reported only for two topical treatments, namely, calcipotriol and corticosteroids. Many antipsoriatic drugs are not licensed for use in children. In addition to disease severity and sites of

involvement, co-morbid conditions like psoriatic arthropathy, hematological, liver and renal function parameters, quality of life and level of social, emotional, or functional disability also influence therapy decision. Systemic therapy can be considered in patients not responding to topical or phototherapy, or in patients having moderate to severe disease.

### *Avoidance/ removal of triggering factors*

Precipitating factors are more significant in children than among adults with psoriasis.<sup>[13]</sup> Children take less drugs and alcohol but are more exposed to trauma and infections. Any form of trauma (via Koebner phenomenon) including physical, surgical, or inflammatory trauma can result in exacerbation of psoriasis. There is a strong association between pharyngitis by group A beta- hemolytic streptococci and the clinical activity of psoriasis, especially guttate psoriasis. There is considerable anecdotal evidence that treating infection improves psoriasis, and for recurrent guttate psoriasis, prophylactic antibiotics or tonsillectomies have been advocated, though controlled trials are lacking.<sup>[23,24]</sup>

## TOPICAL THERAPY

Mostly, topical treatment is sufficient to control the disease in majority of children. The choice of therapy will depend upon morphology, site involved and individual patient's tolerability.

### *Emollients and keratolytics*

Emollients, moisturizers, and keratolytic agents are essential and always play an adjunctive role in the topical treatment of psoriasis. The keratolytic agents, especially salicylic acid, are used in hyperkeratotic lesions, whereas moisturizing products and emollients are especially suitable in the common plaque type scaly lesions, softening thick crusted scales over scalp and as maintenance treatment in the chronic/remission phase of psoriasis.<sup>[25]</sup>

Emollients and moisturizers are beneficial due to their supportive role in normalizing hyperproliferation, differentiation, and apoptosis; furthermore, they exert anti-inflammatory effects, through physiologic lipids. Subsequently, an improved barrier function and stratum corneum hydration, makes the epidermis less amenable to external trauma and stress, thereby reducing the induction of Koebner phenomena. There is some evidence that pretreatment with emollient like

clear mineral or vaseline oil, enhances the therapeutic efficacy of narrow-band ultraviolet-B phototherapy, probably because the oil penetrates the intercellular space allowing an optical matching effect which increases the UV transmission.<sup>[26]</sup>

Salicylic acid (3%, 6% ointment, shampoo) is a useful keratolytic agent that can be used for small, thick, focal plaques, such as those arising on the scalp, palms, and soles in children older than six years. It should be avoided in the infants and toddlers because of risk of percutaneous salicylate intoxication.<sup>[25]</sup>

#### **Coal tar**

Coal tar is a by-product of the destructive carbonization and distillation of coal, roughly comprising 48% hydrocarbons, 42% carbon and 10% water. Coal tar has antiproliferative effects and, like dithranol, modulates inflammatory events in psoriasis.<sup>[27]</sup> It can be compounded in an ointment, cream or solution vehicle in concentrations from 0.5% to 20%. Tar is a safe and effective treatment for childhood psoriasis particularly plaque type lesions. It can be used alone topically or in combination therapy with other medications such as topical corticosteroids, salicylic acid and with UV irradiation. However, it is irritating on the face and flexures, sites frequently affected in children. Some children and parents may find the smell, black color and photosensitizing potential of coal tar as limiting factors in its long-term use.

Liquor carbonis detergens (LCD) used in concentrations from 0.5% to 20% is a modified coal tar prepared by extracting coal tar with alcohol and emulsifying with polysorbate 80. LCD is less clinically active, but is yellow-brown rather than black, and rubs almost invisibly into the skin with a faint residual odor having better cosmetic acceptability. Many modifications have been made to tar preparations to increase their acceptability, as some dislike its odor, messy application, and staining of clothing. Attempts in making lecithinized formulation, owing to its superior non-staining and washability characteristics, may improve the cosmetic acceptability of coal tar maintaining its clinical efficacy.<sup>[28]</sup>

Side effects of tar are primarily cutaneous and include folliculitis, irritant and allergic reactions, photosensitivity, and induction of pustular or erythrodermic reactions if used on acutely inflamed psoriasis. Education regarding its efficacy and good

safety profile and place in therapy as a steroid-sparing adjunct may increase tolerance and compliance of this excellent and underutilized topical therapy.

#### **Dithranol**

Anthralin (dithranol) is a potent anti-inflammatory and anti-proliferative agent. It is a synthetic version of chrysarobin, a natural substance derived from the Araroba tree of South America, used to treat psoriasis for nearly 100 years.<sup>[29]</sup> In contrast to hospital settings, where anthralin in petrolatum base is still used as “long-contact” therapy, in outpatients clinic “short-contact” or “minute” therapy are in practice, to reduce side effects like irritation, temporary perilesional staining of the skin, permanent staining of cloths and improve compliance. Increasing concentrations (0.1% to 3%) of dithranol applied to the skin is left in place for 10-30 minutes daily until a slight irritation develops, then the dose/time is held until lesion clear. Petroleum jelly applied to perilesional skin serves to protect it from irritation.<sup>[29]</sup> This therapy may be applied under careful supervision. In an open study of 58 children, aged 5–10 years treated with dithranol at concentrations up to 1%, remission was achieved in 47 (81%) patients.<sup>[30]</sup> Anthralin therapy can be combined with other topical treatments or UVB phototherapy as in Ingram regimen to improve the response.

#### **Corticosteroids**

Corticosteroids remain among the first line agents in the topical treatment of psoriasis in all age groups.<sup>[31]</sup> They have anti-inflammatory and antiproliferative properties and reduce erythema, scaling, and pruritus in psoriasis. A variety of vehicles are available to choose from, including creams, emollient cream, ointment, gel, spray, lotion, solution, nail lacquer, tape, and foam. The site of application, patient's and parent's preferences determine the choice of appropriate formulation. In general, greasy ointments are recommended at night-time for thick hyperkeratotic plaques, cosmetically acceptable creams can be used in day time, whereas foams and lotions are preferred in scalp psoriasis.<sup>[32]</sup>

Topical corticosteroids are used in chronic plaque type psoriasis as monotherapy or in combination with topical treatments like calcipotriol and tazarotene to reduce their irritation potential. They are also widely used for the disease involving face, ears, flexures and genitals. Usually, lower potencies preparations are indicated for facial, genital and intertriginous skin

areas, whereas thick hyperkeratotic areas, such as the palms and soles, require high potency agents. In general, prolonged use of highly potent corticosteroids should be avoided in children. Strategies to reduce the amount of corticosteroids used are “weekend therapy” or “pulse therapy,” intermittent and rotational therapy as well as combination with other topical treatments such as coal tar, anthralin, calcipotriol, and calcineurin inhibitors.

Side effects of long-term use of topical corticosteroids like skin atrophy and striae at the site of application may occur, particularly in facial, flexural, and genital skin. Application should be slowly tapered off to avoid rebound of psoriasis. In rare cases, especially in infants and small children because of increased skin surface-to-body mass ratio, suppression of the hypothalamic-pituitary-adrenal axis may occur after prolonged, widespread application of potent topical corticosteroids.

#### **Vitamin D3 analogues**

Calcipotriol, tacalcitol, maxacalcitol and calcitriol are vitamin D3 analogues beneficial for psoriasis because of their anti-inflammatory effects, as well as induction of keratinocyte differentiation and inhibition of epidermal proliferation. Calcipotriene (calcipotriol) is an efficient nonsteroidal alternative in the treatment of mild to moderate plaque type psoriasis and has utility as monotherapy, as well as in novel sequential and rotational combinations with topical steroids. In adult clinical trials, its efficacy has been reported to be comparable to or better than class II corticosteroid ointments and anthralin and preferred cosmetically over the latter. An ointment combination of calcipotriene hydrate and betamethasone dipropionate (Daivobet/Dovobet/Taclonex) used as once daily therapy in psoriasis vulgaris has more rapid onset of action as compared with calcipotriol cream alone in short-term treatment, though it is yet to be established in children.<sup>[29]</sup>

In a non-controlled study of 66 children aged 2–14 years, twice daily calcipotriol ointment (50  $\mu\text{g/g}$ ) up to 45 g/week/m<sup>2</sup> for 8 weeks was found to be effective without altering serum calcium. Irritation and facial rashes were no more frequent than in adults.<sup>[33]</sup> In another trial comprising 77 children treated as above but with the ointment base as control, the PASI was reduced by 52% in the treated group and by 37% in the control group.<sup>[34]</sup> There are also case reports of its successful use

in infants without any altered calcium metabolism.<sup>[35,36]</sup> In adults, UVB phototherapy was shown to increase the efficacy of vitamin D3 analogues.<sup>[37]</sup>

The most common side effects are burning sensation or irritation of the skin, especially when used in the flexures and on the face. Application in these areas should be avoided. In the UK, Dovonex cream and ointment (calcipotriol 50  $\mu\text{g/g}$ ) are licensed for use in children with a maximum dose of 75 g/week for children aged over 12 years and 50 g/week for those aged 6-12 years. Newer formulations particularly useful for scalp psoriasis are in gel and solution forms for better patient compliance. There is limited experience with vitamin D3 analogues other than 0.005% calcipotriol in children with psoriasis.

#### **Tazarotene**

The topical retinoid tazarotene has recently been licensed for use in adult patients with psoriasis, but as yet there are no data on the efficacy and safety in children. It is available in 0.05% and 0.1% gels, and a cream formulation has also been developed. Similar to other retinoids, tazarotene restores normal epidermal differentiation and proliferation and reduces epidermal inflammation. Dose-related skin irritation is common and often necessitates combination with a topical steroid applied at the same or different time of day to decrease irritation and improve overall efficacy. It is preferable to limit its use to thicker plaques on non-intertriginous sites. Short contact (10-60 minutes per day), alternate day or weekly applications are potential ways to include this useful agent in sequential and rotational regimens. There is a case report of beneficial role of tazarotene 0.05% gel applied once daily for 8 weeks for nail psoriasis in a child resulting in clinical improvement particularly subungual hyperkeratosis.<sup>[38]</sup>

#### **Calcineurin inhibitors**

Tacrolimus (0.03%, 0.1%) ointment and pimecrolimus (1%) cream are nonsteroidal immunomodulating macrolactams that act by blocking the enzyme calcineurin thereby inhibiting the production of IL-2 and subsequent T-cell activation and proliferation.

Both topical agents are currently FDA-approved for second-line intermittent treatment of atopic dermatitis in children. Their efficacy has also been recently documented for psoriasis in children.<sup>[39,40]</sup> Tacrolimus and pimecrolimus are effective, safe and

well-tolerated therapeutic options for thin patches and plaques of psoriasis at sites more susceptible to the long-term adverse effects of topical steroids, such as the face, flexures, and anogenital region and also provide useful option to be used in sequential and rotational regimens.

## SYSTEMIC THERAPY

There are no controlled trials of systemic drugs for psoriasis in this age group but the most documented experience appears to be with retinoids which are probably considered as second-line drug of choice for children. Methotrexate and cyclosporine appear to be effective in children but more efficacy and safety data are required. Many of the treatments used in adults have been tried in children but are not licensed in this age group. All these therapeutic options can be used as monotherapy or in various combinations with topical or systemic drugs.

Systemic therapy should only be considered in severe forms of the disease such as extensive plaque type psoriasis, erythroderma, pustular psoriasis, psoriatic arthritis or any form refractory to topical and phototherapy. Pustular and erythrodermic psoriasis may settle with bland topical treatment and hospitalized supportive care unless very severe. However, because of rarity of severe forms of disease in this age group, there is relatively less information with no guidelines or consensus on the use of systemic therapies in childhood psoriasis and it is used mostly empirically. Lower tolerability and cumulative toxicities also limit their use in children.

### Methotrexate

Methotrexate (MTX) is an antimetabolite agent, having immunomodulatory and profound anti-inflammatory properties. Since late 1950s, MTX is the gold standard therapy in psoriasis and in era of biological treatments, it continues to be an agent with which other systemic psoriasis medications are compared.<sup>[41]</sup> The advantages of MTX are its efficacy, affordability and convenient weekly oral dose. In children, 0.2 mg/kg to 0.4 mg/kg per week orally is the recommended therapeutic dose range.<sup>[32]</sup> Parenteral administration (subcutaneous, intravenous, intramuscular) is advised if adequate oral dosing is ineffective as the absorption spectrum among individuals can vary substantially or to overcome gastrointestinal side effects like nausea and vomiting.

Meticulous use of MTX may avert the long term or serious side effects. The tolerability and efficacy of MTX in the treatment of childhood psoriasis has been documented in few case series. Kumar *et al.*<sup>[42]</sup> first reported successful use of MTX in 7 children (3 to 16 years of age) having severe disease without any significant side-effects or biochemical and hematological alterations. Dogra *et al.*<sup>[43]</sup> have documented excellent therapeutic outcome in a 2-year-old child with generalized pustular psoriasis. In a study of 24 children with severe psoriasis from India, response to treatment with oral MTX (0.2-0.4 mg/kg one weekly dose) was excellent (>75% decrease in PASI) in all but two patients. The mean time to control the disease, i.e., 50% reduction in PASI was 5.1 weeks. Side effects were mild, observed in nine children, which included nausea, vomiting, and loss of appetite.<sup>[44]</sup> Another recently published study from UK reported 11 out of 13 children with severe plaque type psoriasis treated with low dose oral once weekly MTX (0.03–0.24 mg / kg, increased to 0.1–0.41 mg / kg) responded with clearance of psoriasis leaving small residual plaques. It was well tolerated except for abnormal liver function tests in 2 patients.<sup>[45]</sup>

MTX is an effective, cheap, easily available, and reasonably safe drug to be used in severe childhood psoriasis. It can be a promising therapeutic option in gaining control in the acute phases or flares of the disease, followed by transition to more conventional topical or UV light-based maintenance regimens. MTX is associated with a substantial number of potential side effects, most significantly hematological, hepatotoxicity, and drug interactions which requires vigilant clinical and laboratory monitoring as per the standard guidelines.<sup>[46]</sup> Considering the long-term safety concerns in children, use of systemic agents like MTX should be undertaken only by experienced dermatologists with adequate facilities for monitoring. As hepatic toxicity of MTX is related to total cumulative dose, it should generally be avoided in children who may require many years of systemic therapy in future.

### Retinoids

Acitretin is an aromatic retinoid that acts in psoriasis by its anti-inflammatory activity, and modulating epidermal proliferation and differentiation. It is considered to be beneficial particularly in severe pustular psoriasis. Treatment should be initiated and maintained at dosages at or below 0.5 mg/kg to 1 mg/

kg per day to limit short- and long-term toxicities. When significant improvement occurs, the initial dose should be gradually tapered until a dose of 0.2 mg/kg per day and therapy should be continued for about 2 months after clinical remission. Acitretin is available in 10-mg and 25-mg gelatin capsules and oral administration with milk or fatty foods enhances absorption.<sup>[46]</sup> Acitretin is a slow acting therapy in plaque type psoriasis associated with gradual clearance of lesions; hence, it may be best suited for longer-term maintenance therapy or as a part of a sequential treatment regimen with UVB or cyclosporine.<sup>[47-49]</sup>

The major limitation of oral retinoids (acitretin) in children is the risk of growth retardation due to premature closure of epiphyses on long-term use. But unlike in ichthyosiform disorders, continuous treatment over such periods may not be necessary in psoriasis. Besides its highly teratogenic potential, the most common adverse events are mucocutaneous (xerosis, cheilitis, skin fragility, epistaxis) and minor reversible alterations in liver enzymes and lipids, which rarely necessitate cessation of therapy.<sup>[46]</sup>

#### Cyclosporine

Cyclosporine (CYA) primarily acts by inhibiting T-cell function and interleukin (IL)-2. It is effective in severe forms of psoriasis such as pustular or erythrodermic psoriasis or when other therapies are ineffective and is often used as a short-term crisis management drug.<sup>[50-52]</sup> It can be used as single or intermittent short courses as monotherapy and in combination or sequential therapy with other topical and systemic therapies. Most of the reports indicate a favorable response with CYA in childhood psoriasis; however, Mahe *et al.* reported 4 cases, in none of whom it was found to be effective.<sup>[53]</sup> The rate of improvement depends very much on the dose, which ranges from 3 to 5.0 mg/kg/day. The dose should be tapered gradually to the lowest dose needed to maintain disease control. Pharmacokinetics of CYA including intestinal absorption, distribution in body fluids and tissues, metabolism and elimination is different in children, thus requiring higher doses for similar therapeutic effects with potential risk of dose dependent toxicity.

Dosage adjustments are based on monitoring of clinical response, serum creatinine levels, and blood pressure. Its use is limited by the risk of nephrotoxicity, hypertension and immunosuppression apart from other mucocutaneous side effects. In carefully

selected and closely monitored patients, cyclosporine can produce relatively rapid clinical response and can be effectively combined with topical and systemic therapies to increase its efficacy and decrease end organ toxicity.

#### Hydroxyurea

There has been a renewed interest on the use of hydroxyurea in Indian patients with psoriasis;<sup>[54,55]</sup> however, experience regarding its use in the treatment of childhood psoriasis is limited. Hematological side effects are of concern in this age group.

#### Biologics

Biologics are group of drugs including antibodies and fusion proteins targeting cytokines like tumor necrosis factor  $\alpha$  that play an important role in the pathogenesis of psoriasis. Etanercept has been found to be overall effective and well tolerated in children and adolescents with moderate-to-severe plaque psoriasis.<sup>[56-58]</sup> There are two case reports on the use of infliximab in pediatric psoriasis with good results.<sup>[59]</sup> Although further experience is warranted, infliximab appears promising for the treatment of refractory plaque and generalized pustular psoriasis in children. Other biologics have not been tried in childhood psoriasis yet. Although these new therapeutic agents appear promising in refractory and severe childhood psoriasis, their benefit has to outweigh potential risk of infection, lymphoma and demyelinating disorders.<sup>[59]</sup> There are currently no guidelines for the use of biological agents for psoriasis in pediatric age group and cost is a major limiting factor in most of the developing nations.

#### Phototherapy

Phototherapy is appropriate for carefully selected patients with refractory disease, diffuse (>15%–20% BSA) involvement, or focal debilitating palmoplantar psoriasis. Three main types of therapeutic light options exist: broadband UVB (BB-UVB, 290–320 nm), narrowband UVB (NBUVB, 311  $\pm$  2 nm) and UVA (320–400 nm). They are useful in psoriasis by their action of inhibiting DNA synthesis and epidermal keratinocyte proliferation, induce T-cell apoptosis and immunosuppressive and anti-inflammatory cytokines.<sup>[60]</sup>

Generally phototherapy is preferred in older children and adolescents with moderate to severe disease in which topical treatments have failed. Guttate and thin plaque type lesions respond best to phototherapy. It

is often not suitable for small children and infants because of potential early side effects like erythema and burning, need of frequent hospital visits and their poor compliance in standing within closed UV chambers.

Studies comparing NB-UVB and PUVA (psoralens + UVA) report PUVA being more effective in psoriasis.<sup>[61]</sup> In children, NB-UVB is more convenient and may be less carcinogenic, and given the independence of psoralens-related precautions and adverse effects, NB-UVB is now considered first-line phototherapy in pediatric age group for psoriasis.<sup>[62]</sup> To limit the cumulative UVB dose and thereby the carcinogenic risk, combination with systemic therapy like acitretin<sup>[49]</sup> or topical therapy like calcipotriol, tazarotene and anthraline has been found useful.<sup>[63]</sup> PUVA is used with extreme caution in children less than 12 years. Many investigators consider oral PUVA relatively contraindicated in children less than 12 years and because of the many short- and long-term toxicities associated with psoralen ingestion including nausea, vomiting, headache, hepatotoxicity, photosensitization requiring photoprotection, ocular toxicity, acute risk of burning, and long-term risk of skin cancer.

PUVA bath treatment should be preferred to oral PUVA in older children (>12 years) and adolescents in situations like recalcitrant hand and foot psoriasis because of avoidance of gastrointestinal side effects, lack of eye protection required, and shorter photosensitization time.<sup>[62]</sup>

In the absence of any clear evidence concerning the long-term safety of UVB, it should be used with appropriate precautions and guidelines in children. Parents should be advised that there may be a slight increase in photoaging and risk of skin cancer over long-term treatment. UV treatment to children must be administered in an appropriate environment with constant supervision by parents and trained professional staff. A pilot study has reported 308 nm excimer laser to be a safe and effective treatment for localized psoriasis in children as in adults.<sup>[64]</sup>

## CONCLUSION

Childhood psoriasis represents a special challenge to dermatologists. Limited data suggests that psoriasis in Indian children differs from western countries in having

a later onset, equal sex distribution, infrequent facial involvement, low frequency of guttate lesions, more frequent involvement of the soles, and a low incidence of familial occurrence. Besides proper treatment of the disease considering the clinical presentation and the age of the patient, management of these patients has to include supportive care and consider quality of life issues like psychosocial stigmas. Most children have mild to moderate psoriasis for which topical treatment is often sufficient. Recurrences are common adding to long-term morbidity over life. New innovations in topical and systemic therapy, phototherapy and biologicals may provide promising future in psoriasis therapeutic armamentarium.

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