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REVIEW ARTICLE

Optimizing the treatment of atopic dermatitis in children: a review of the benefit/risk ratio of methylprednisolone aceponate

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Abstract

Atopic dermatitis (AD) is a chronic, recurring, pruritic, inflammatory skin condition which has its onset in early childhood in most cases. A stepped approach to therapy, starting with emollients and adding first mild and then more potent topical medications is recommended. For more than 50 years, topical corticosteroids (TCs) have been the gold standard in AD therapy. Increasingly potent TCs have tended to come with increasing risk of adverse events, however. Calculating the benefit/risk ratio [or therapeutic index (TIX)] for TCs when treating children and infants is more challenging in this population. Not only does their increased surface area to volume ratio as a result of their small size mean that they are likely to absorb a greater proportion of any active agent applied to their skin, but drug metabolism is slower than in adults and the systemic effects of corticosteroids are more pronounced (in particular reduction of serum cortisol levels through suppression of the hypothalamic–pituitary–adrenal axis). Unlike traditional TCs, topical calcineurin inhibitors are not associated with the systemic effects and have shown good efficacy in treating AD in children. Parental/Carer concerns about their long-term use can limit their acceptance for treatment in the paediatric population, however. Modifications to the structure of fourth generation corticosteroids mean that increased potency is not accompanied by increased risk of adverse events and hence they have an improved TIX. Methylprednisolone aceponate is a potent fourth generation corticosteroid which has demonstrated efficacy and safety in acute and maintenance programmes in infants and children. It is licenced for once-daily use, and is available in four formulations – ointment, fatty ointment, cream and milk, which combine with its improved TIX to meet the needs of young patients and their carers.

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Keywords

atopic dermatitis, calcineurin inhibitors, methylprednisolone aceponate, MPA, therapeutic index

Conflict of interest

U. Blume-Peytavi and U. Wahn are consultants for Intendis/Bayer with a vested interest in the product being studied, and on issues related and unrelated to the product being studied.

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Introduction

Atopic dermatitis (AD) is a chronic, recurring, pruritic, inflammatory skin condition which has its onset in early childhood in most individuals and has an important impact on life quality.[1] Approximately 80% of paediatric AD cases present before the age of 1 year, with a furthermore 10% presenting before the age of 2 years.[2] AD is seen in infants from the age of approximately 3 months, while infantile seborrhoeic dermatitis causing skin scaling and crusting (though not pruritus) may be observed even earlier, from the age of below 4 weeks.

The skin of children with AD undergoes some key changes, disturbing its barrier function, increasing trans-epidermal water loss, reducing stratum corneum hydration and resulting in dry, cracked skin that facilitates the penetration of allergens and

microbial antigens.[3] Disturbed sweat gland and sebaceous gland activity/function furthermore reduces the normal skin barrier function, leading to reduced regulative and protective abilities. This finding has a significant impact on a patient's ability to regulate body temperature, potentially exacerbating symptoms. Accumulation of by-products of the inflammatory process in the dermis and epidermis result in changes to both macro and microcirculation.[3] Effective control of infantile AD is essential to reduce the severity and duration of flares, and to facilitate long-term maintenance. Rapid treatment of acute flares and maintenance of symptom-free skin can help to prevent chronic manifestations of AD. It can be assumed that treatment of AD in children will need to continue over a number of years, although there is a trend towards spontaneous improvement with increasing age.[2]

There appears to be a genetic element in many cases of eczema/AD; children of parents with atopic disease are much more likely to have an exaggerated inflammatory response to environmental triggers than those whose parents are unaffected.[4–6] Based on the results of a number of studies and analyses,[7–11] a recent joint consensus paper from the American Academy of Allergy, Asthma and Immunology and European Academy of Allergy and Clinical Immunology concluded that AD – along with other clinical manifestations of atopy, such as the presence of elevated total immunoglobulin E levels – is a risk factor for occurrence, severity and persistence of childhood asthma.[12] As asthma is the most common chronic disease among children in nearly all industrialized countries, this so-called 'Atopic March' creates an additional imperative for prompt and effective control of AD. Eczema has a significant impact on quality of life – and in the case of children with eczema, this can extend to other members of the family. AD can curtail children's enjoyment of swimming and other outdoor activities, and may require them to alter their diet to avoid substances that trigger symptom flares. Itching can result in loss of sleep leading to lack of attentiveness in school. Skin lesions can cause embarrassment and discomfort; control of lesions assumes more importance in older, more self-aware children. Severe AD can result in restriction of normal daily living, including schooling and social isolation. It is self-evident that effective management is an important goal.

Stepped approach to management of AD in children

The primary goals of therapy are to relieve symptoms, to reduce the severity and duration of acute exacerbations, and to protect and maintain the skin barrier. Management focuses on appropriate moisturization of the skin, treatment of flares and avoidance of factors that exacerbate the condition. Akdis advocates a stepped approach to care (Fig. 1), beginning with regular application of emollients in children with mild AD[13] and adding anti-inflammatory medicines and other measures in more severe cases.

Emollients

Emollients (moisturizers) provide a protective film over the skin, keeping moisture in and irritants out. They act by preventing water loss from, and by directly adding water to, the outer skin layers.[1] NICE guidelines recognize emollients as the most important treatment for AD because they restore the defective skin barrier, and they recommend that emollients form the basis of AD management.[1] Emollients are available in a variety of formulations, including ointments, creams, lotions, gels, aerosol sprays and bath oils. They can be used as moisturizers, as soap substitutes for cleansing the skin and as bath oils for bathing. Children with AD should use a range of different emollients, including a topical formulation and a wash product. They should be offered the opportunity to try different products and combinations of products. The choice of emollient formulation will depend on the skin status, the climate and the individual patient's needs, preferences and tolerance. Emollients should be applied frequently (at least daily) and in large quantities, even if the skin is clear.[1,14]

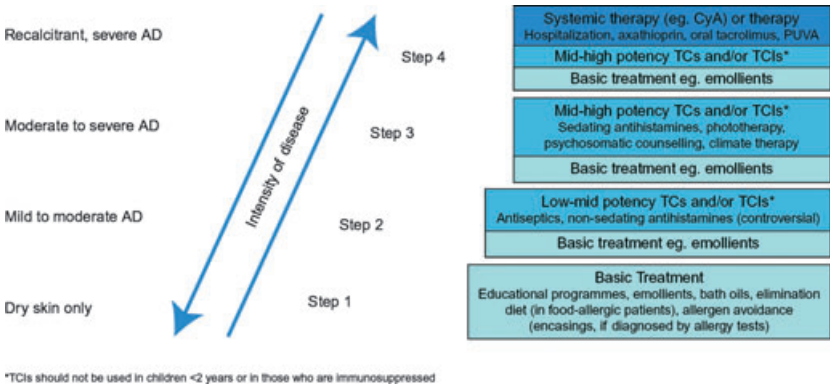

Figure 1 Stepwise management of patients with AD treatment should be escalated according to the severity of AD symptoms. AD, atopic dermatitis; CyA, cyclosporin A; PUVA, psoralen plus ultraviolet A treatment; TCs, topical corticosteroids; TCIs, topical calcineurin inhibitors. Adapted from Akdis *et al.*[13]

Topical therapies – getting the benefit/risk ratio in balance

The therapeutic index (TIX) describes the balance between potency and adverse events of topical corticosteroids (TCs) (see Fig. 2) – i.e. the benefit/risk ratio.

The optimization of efficacy, potency and safety is a key goal of any therapy, but achieving the appropriate TIX can present challenges in children, particularly when applying topical medications. The small size of infants and children means that the ratio of skin surface area to body weight is much greater than that in adults, and infants skin permits localization dependent higher penetration rates of topically applied medications leading to significantly higher drug levels.[15] Bioavailability studies have suggested that that both the passive and active transport processes are not fully mature in children until the age of 4 months.[16] This potential for increased risk of adverse effects means that, in children with AD, topical anti-inflammatory agents to treat acute flares should be chosen carefully to maximize the therapeutic effect, should be used for a minimum duration of time and should be monitored carefully.

Topical corticosteroids

Topical corticosteroids, which reduce inflammation and alleviate symptoms, have been the gold standard of treatment for AD for over 50 years.[1,14] Cortisol, the original corticosteroid, has undergone numerous modifications to achieve improved skin penetration by increasing lipophilicity (e.g. by esterification at C-17 and/or C-21) and increasing glucocorticoid receptor binding (methylation and/or halogenation at C-6 and C-9). In earlier developed therapeutics, increases in potency have been matched by increases in the incidence and severity of adverse effects, including systemic effects following absorption into the bloodstream. Halogenated corticosteroids in particular have been shown to reduce plasma cortisol levels and adversely affect the normal circadian rhythm of cortisol release via suppression of the hypothalamic–pituitary–adrenal axis. Non-halogenated corticosteroids exert a negligible influence on endogenous cortisol levels and preserve the function of the circadian rhythm of cortisol secretion.[3]

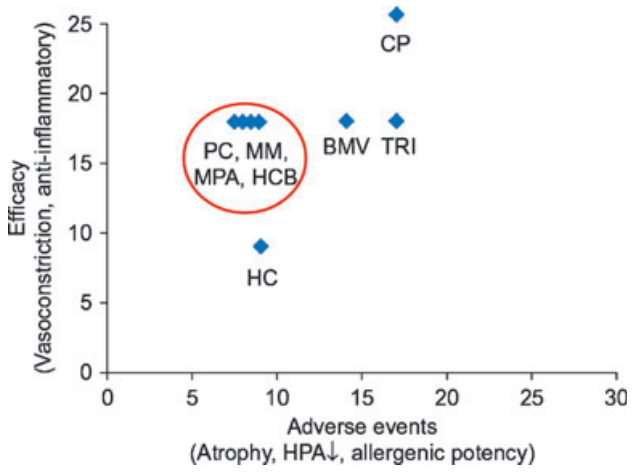

Figure 2 A representation of efficacy vs. adverse events [therapeutic index (TIX)] for a number of topical corticosteroids. The clinical compounds (PC, MM, MPA, HCB) have a TIX of 2.0 indicating a very favourable efficacy to adverse events rate. BMV, betamethasone valerate; CP, clobetasol propionate; HC, halcinonide; HCB, hydrocortisone butyrate; HPA, hypothalamic–pituitary–adrenal; MM, mometasone furoate; MPA, methylprednisolone aceponate; PC, prednicarbate; TRI, triamcinolone acetonide. Adapted from Luger *et al. JDDG* 2004; **2**: 629–634.

This potential to suppress the hypothalamic–pituitary–adrenal axis is significant in children and infants because of their higher surface area to body weight ratio.[15] Turpeinen and colleagues have demonstrated a clear correlation between decreasing age and percutaneous absorption of hydrocortisone in young children, with a significantly higher serum cortisol rise detected in children aged below 18 months compared with those aged 18 months or over.[17]

Concern about the safety of corticosteroids in children can lead doctors to prescribe lower potency medications and carers to be reluctant to apply the medication.[18] This practice can result in poor symptom control and reduced quality of life. Alternatives to traditional corticosteroids – such as calcineurin inhibitors and fourth generation corticosteroids – are available and are discussed below.

Choice of vehicle

The choice of TC vehicle should be tailored to the clinical stage of eczema and the patient's/carer's preference. Vehicles are in general classified as 'hydrophilic' (e.g. water, isopropanol, glycerol) or 'hydrophobic' (e.g. petrolatum, liquid paraffin, palmitates).[19] Depending on the vehicle(s) used, preparations may be classified as liquids (hydrophilic solutions, lipophilic or hydrophilic lotions and liquid emulsions) or semi-solids (hydrophilic or hydrophobic creams and ointments). Hydrophobic ointments (or 'fatty ointments') have occlusive properties, which increase the penetration of the product into the dermis and are essential for treating dry eczema;[20] however, they can be difficult to apply to the skin of infants because they have to be rubbed in.[20] Ointment bases in general are preferred for infiltrated, lichenified lesions as they enhance penetration and hydrate the stratum corneum. Creams are preferred for acute and sub-acute dermatoses and on moist or intertriginous areas.[21] Water-based products with astringent properties are ideal for treating exudative eczema and lesions.[2] Lotions and milks are gentle enough for treating infant skin and are mainly indicated in times and areas with warm temperatures. A number of TCs licenced for use in eczema/AD are available as more than one type of preparation, typically as a cream and an ointment, sometimes also as a lotion.[21] Despite the classical water-oil concept, more recently other new formulations were brought to market by several manufactures and with various active

ingredients, e.g. an ethanol free emulsion foam vehicle containing desonide 0.05%.

Topical calcineurin inhibitors

Topical calcineurin inhibitors (TCIs) – such as tacrolimus and pimecrolimus – are non-steroidal inhibitors of inflammatory cytokines and thus provide an alternative to corticosteroids for doctors, patients and carers with concerns about the latter's safety.

In clinical studies in infants, onset of therapeutic effect has been observed within a few days of starting treatment with pimecrolimus.[22,23] Tacrolimus is effective at reducing the symptoms of severe AD.[24] TCs can be added to TCIs to improve control of AD flares if required.[25,26]

Unfortunately, up to now, calcineurin inhibitors have only been available as a single galenic preparation, not enabling the choice of galenic preparation to be adapted to the infant's skin condition and the localisation of the eczema.

In a meta-analysis conducted by Ashcroft and colleagues, topical tacrolimus proved more efficacious than topical pimecrolimus in patients with AD.[27] It has also proved more efficacious than corticosteroids with mild to moderate potency in adults and children,[24,27–29] and to have comparable efficacy with potent corticosteroids in adults and children with AD.[27] In one large study involving children aged 2–15 years with moderate-to-severe AD, tacrolimus (0.03%) ointment applied once or twice-daily gave significantly ($P < 0.001$) greater reductions in modified Eczema Area and Severity Index (mEASI) scores than hydrocortisone acetate (1%) ointment applied twice-daily.[28] The greatest reductions in mEASI scores were observed when children were treated twice-daily with tacrolimus ($P = 0.001$ vs. once-daily treatment).

Safety of calcineurin inhibitors

In clinical studies in infants and children, tacrolimus and pimecrolimus have proved to be in general well tolerated, with few study-related adverse events. Infants with up to 92% of their body affected by AD treated with topical pimecrolimus for 3 weeks experienced minimal (typically <2 ng/mL blood) systemic exposure to the drug.[23] Similarly, in a study in infants aged 3–24 months with up to 40% of their body affected by AD treated with tacrolimus for 14 days, plasma concentrations of tacrolimus were minimal (<1 ng/mL) but were higher in the smallest patients.[30]

As a result of the immunosuppressant activity of these drugs there are concerns about their potential to promote skin infections and malignancies following long-term treatment.[31] In 2005, this led to the inclusion of a black box warning on the labels of topical tacrolimus and pimecrolimus indicating that long-term safety had not been established.

At the FDA's request, long-term paediatric registries to investigate concerns about long-term use were established in 2005/6.

In a US cohort study of 92 585 pimecrolimus initiators contributing 121 289 person-years of follow-up, 26 lymphomas were identified (incidence of 21/100 000 person-years).[32] This incidence of lymphoma was similar to that among tacrolimus users (rate ratio, RR = 1.16; 95% confidence interval, CI = 0.74–1.82). No increase in risk of lymphoma among initiators of topical pimecrolimus relative to other topical agents during an average follow-up of 1.3 years was found.

Moving forward – fourth generation corticosteroids with improved TIX

The fourth generation corticosteroids include aclometasone, budesonide, fluticasone propionate, hydrocortisone aceponate, hydrocortisone-17-butyrate-21-propionate, methylprednisolone aceponate, mometasone furoate and prednicarbate. The structures of these molecules are designed to dissociate potency from toxicity, resulting in an increased TIX.

Most members of the group are potent anti-inflammatory agents and several have been studied in paediatric trials. Treatment is typically given for only up to 21 days (shorter periods in infants). Symptom relief is rapid and success rates are in general greater than 80% with creams, ointments and lotions. Aclometasone 0.05% treatment is associated with complete clearing of monitored signs and symptoms in 72% of children treated,[33] and has comparable efficacy to hydrocortisone butyrate 0.1% and clobetasone butyrate cream 0.05%.[34,35] Clobetasone is also comparable to fluticasone propionate 0.05%[36] but less efficacious than mometasone furoate 0.01%.[37] Intermittent treatment strategies can reduce the need for acute intensive courses, providing greater 'steroid-sparing' potential.[38] For example, stepping down the frequency of dosing from daily to just a few times a week led to a reduction in the incidence of flares.[38–40]

Suppression of cortisol levels, including in long-term studies, was only rarely seen,[2,33,36,41–44] although prednicarbate is not recommended for use under occlusive conditions (including in the diaper area in infants) because it increases cortisol suppression under these conditions.[44,45]

These paediatric studies indicate that these newer corticosteroids have equal or greater efficacy with older corticosteroids and equal or lower incidence of adverse events (depending on the potency of the older corticosteroid).[34,35,43,44,46]

Methylprednisolone aceponate is safe and effective in paediatric patients

Like other fourth generation corticosteroids, methylprednisolone aceponate (MPA) is rapidly absorbed because of its increased lipophilicity. It is metabolized by skin esterases to produce the more active metabolite methylprednisolone propionate (MPP). Once MPP dissociates from the glucocorticoid receptor, it undergoes rapid deactivation, making it unavailable for absorption into the systemic circulation.[47]

The MPA is classified as a potent corticosteroid. A number of studies have investigated its efficacy and safety in children with mild, moderate as well as severe AD (see Table 1).

Table 1 Comparisons of levels of evidence* for efficacy and safety of MPA in children with atopic dermatitis

Description of study	*N*	Ages of children	Level of evidence	References
Multicentre, double-blind RCT with MPA 0.1% ointment QD vs tacrolimus 0.03% ointment BID in acute severe AD; duration ≥2 weeks, ≤3 weeks; endpoints based on changes in EASI, IGA, DLQI and CDLQI	129 vs. 136	2–15 years	I	48
Multicentre, double-blind RCT with MPA 0.1% cream twice weekly vs. emollient only in stabilized acute severe to very severe AD; duration 16 weeks	112 vs. 109	>12 years	I	40
Multicentre, double-blind RCT with MPA 0.1% cream BID vs. PC 0.25% cream BID in AD; duration ≤21 days	38 vs. 40	3–14 years	I	43
Multicentre, double-blind RCT with MPA 0.1% ointment QD plus vehicle QD vs. PC 0.25% ointment BID in AD; duration ≤21 days	55 vs. 53	4 months–14 years	I	43
Multicentre, double-blind, randomized safety study with MPA 0.1% ointment BID vs. HCB 0.1% cream BID in AD; 12-day study with 2-day run-in phase, 7 days on treatment and 4-day wash-out phase	10 vs. 10	6 months–12 years	I	43
Multicentre, open-label, prospective, randomized, comparative study with MPA 0.1% cream QD vs. MMF 0.1% cream QD in acute or subacute mild or moderate AD; duration ≥1 week, ≤4 weeks	69 vs. 68	2–14 years	I	49
Double-blind, non-randomized bilateral safety study with MPA 0.1% cream BID vs. PC 0.25% cream in AD BID; duration 3 weeks	38 vs. 40	3–14 years	IIi	50
Double-blind, non-randomized bilateral safety study with MPA 0.1% fatty ointment vs. BMV ointment in AD; duration 4 weeks	40 vs. 40	3–14 years	IIi	50
Single centre, open-label, uncontrolled study with MPA 0.1% ointment QD; patients stratified as having mild, moderate or severe AD; duration ≤21 days depending on disease severity; final analysis based on changes in SCORAD	51	6 months–15 years	IIii	3
Single centre, open-label, uncontrolled study with MPA 0.1% ointment QD in mild, moderately severe or severe AD†; duration 2–4 weeks; final analysis was based on physician assessment	28	4 months–12 years	IIii	51
Multicentre, observational open-label, uncontrolled study with MPA 0.1% ointment, 0.1% cream and 0.1% milk in AD; duration 3 weeks with cream and ointment, 2 weeks with milk; final analysis based on subjective and objective patient/carer and physician assessment	443	<15 years	IIii	52
Single centre, open-label, uncontrolled study with MPA 0.1% milk QD in acute or subacute AD; duration ≤14 days; final analysis based on parent's assessment	27	2 months–4 years	IV	2

*For explanation of levels of evidence, please see Table 2.

†Patients with moderately severe or severe AD received concomitant oral antihistamines, sedatives and tar-based ointments.

AD, atopic dermatitis; BID, twice per day; BMV, betamethasone valerate; CDLQI, children's Dermatology Life Quality Index; DLQI, Dermatology Life Quality Index; EASI, Eczema Area and Severity Index; HCB, hydrocortisone-17-butyrate; IGA, Investigator's Global Assessment; MMF, mometasone furoate; MPA, methylprednisolone aceponate; PC, prednicarbate; QD, every day; RCT, randomized controlled trial; SCORAD, SCORing Atopic Dermatitis.

In one study, MPA (0.1%) ointment and tacrolimus (0.03%) ointment gave comparable reductions in Investigator's Global Assessment (IGA) and EASI scores in children and adolescents with severe dermatitis treated for 14–21 days.[48] MPA gave superior control of itching, greater improvements in quality of sleep and greater reductions in EASI scores than tacrolimus, however.

Table 2 Levels of evidence

Level	Definition
I	Evidence from at least one properly designed randomized, controlled trials
IIi	Evidence from well designed controlled trials without randomisation
IIii	Evidence from well designed cohort or case control analytic studies, preferably from more than one research centre or group
III	Opinions of respected authorities based on clinical experience, descriptive studies or reports of expert committees
IV	Evidence inadequate as a result of problems of methodology (e.g. sample size or length or comprehensiveness or follow-up or conflicts in evidence

Source: Adapted from Stevens A, Raferty J, eds. *Health Care Needs Assessment*. Radcliffe Medical Press, New York, 1997, 304 p.

Moreover, because MPA (0.1%) ointment is applied once-daily while tacrolimus (0.3%) ointment is applied twice-daily, the cost of treatment with MPA was significantly ($P = 0.0001$) lower.[48]

Patients aged 6 months to 15 years with severe AD (SCORing of Atopic Dermatitis score or SCORAD >40) treated with MPA (0.1%) ointment for up to 21 days had reductions in mean SCORAD scores of >90%. Itching was significantly reduced by day 9 and was absent at day 14; erythema and oedema also resolved within 10 days and lesions cleared within 21 days.[3]

In comparison with other corticosteroids, once-daily applications of MPA (0.1%) ointment to children aged 4 months to 14 years were as efficacious as twice-daily applications of prednicarbate.[43] Both medications gave a response rate of >95%.

Following stabilization of acute AD, MPA can be applied at reduced frequency (e.g. twice weekly) along with daily emollients to prevent relapses. Following stabilization of an acute severe or very severe AD flare with MPA cream, 221 patients aged over 12 years entered a 16-week maintenance phase during which they received either MPA 0.1% cream twice weekly plus emollients or emollients only.[40] Time to relapse was greater in the MPA arm than in the emollient arm; patients treated with MPA twice weekly had a 3.5-fold lower risk of relapse than patients treated with emollient alone (95% CI = 1.9–6.4; $P < 0.0001$). At the end of the maintenance phase, patients treated with MPA also had lower EASI, IGA, Dermatology Life Quality Index (DLQI) and children's DLQI scores than controls, indicating reduced intensity of itching and overall improved patient status.[40] The period of treatment can be shortened in patients with less severe disease. Among patients treated with MPA (0.1%) ointment, those with mild or moderate disease (i.e. SCORAD scores ≤20 or ≤40, respectively), saw resolution of symptoms within 14 days. Patients with mild AD experienced resolution of itching, oedema and erythema within a week.[3]

The addition of emollients to the once-daily MPA regimen enhances and prolongs the effect of treatment, resulting in significantly greater improvement in xerosis ($P < 0.001$) and a trend towards faster resolution of pruritus than in patients treated with MPA (0.1%) QD with no additional emollients.[53]

Choosing the best formulation of MPA for paediatric patients

It is difficult to prevent adults with AD from scratching and it is even harder to prevent infants with the condition from scratching. Thus, a key priority in the management of pruritic eczema is to rapidly soothe irritated skin to prevent furthermore damage, furthermore superinfection, disturbed sleep and reduced quality of life.

Methylprednisolone aceponate is available in four formulations – ointment, fatty ointment, cream and milk.[54] Few clinical studies have directly compared the safety and efficacy of different formulations of the same corticosteroid, although a number of studies have compared different formulations of MPA in acute and chronic AD of varying severity.[43,54,55] These have shown that, regardless of formulation, patients rapidly (within a week) experience relief from their symptoms – in particular pruritus and erythema. A majority of patients experience complete remission by the end of treatment (2–3 weeks).[43,54,55] All formulations of MPA are in general well tolerated, with mild burning being the most frequent event. Importantly, cortisol levels remain within the normal range following treatment and circadian rhythm is preserved.[43] The milk formulations of MPA are ideal for children as young as 4 months.[2]

Different formulations of MPA can be used interchangeably and simultaneously (in different areas of the body or where the skin condition differs at different sites necessitating different galenic preparations). Kungurov and colleagues demonstrated that cream applied to face, neck and skin flexures with weeping eczema and oedema reduced mean SCORAD scores by 80% after 12–14 days treatment.[56] Similar results were obtained with ointment applied to areas of dry skin with inflammation, infiltration and lichenification in the same patients. Most children (81%) experienced complete remission of symptoms and no child experienced an adverse event. Interestingly, onset of activity was faster in children than in adults.[56]

Summary and conclusions

Atopic dermatitis affects 15–20% of children in the developed world and can be a debilitating disease with extreme effects on quality of life in the most severe cases. It can also have long-term sequelae, including a higher propensity for asthma and irreversible changes to the skin barrier.

Topical corticosteroids are the gold standard of treatment for AD, but they must be used with care in children, especially in infants whose higher surface area to body weight ratio and age-dependent maturation of the skin barrier function leaves them vulnerable to over-dosing. Suppression of cortisol levels and of the circadian rhythm of cortisol secretion are of more significance in children because of the potential for impeding normal growth and inducing Cushing's syndrome.

Alternatives to traditional TCs, including calcineurin inhibitors and fourth generation corticosteroids, are available. These achieve potent control of AD without the systemic effects associated with traditional corticosteroids. MPA (Advantan®, Intendis/Bayer, Berlin, Germany), a fourth generation corticosteroid, provides rapid and efficacious relief of signs and symptoms of AD with low incidences of topical and systemic side effects in adults and children. The results from numerous studies offer high-grade evidence that MPA provides the optimal benefit-risk-ratio for the treatment of AD in children. It is suitable for once-daily dosing, with the potential for improved compliance and decreased treatment costs compared to medications that require twice-daily dosing. Moreover, it is available in a range of formulations, providing greater choice for patients and their carers. Evidence-based medicine and clinical experience support MPA as a favourable choice for the treatment of AD in children.

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