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ARTICLE

Treatments for atopic dermatitis

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SUMMARY

Atopic dermatitis usually develops in childhood, but can occur in adults. Management involves drug and non-drug treatments to clear the skin.

Not all patients with atopic dermatitis have allergies. Most patients have trigger factors that can be avoided.

All patients should use soap substitutes and bath oils. Moisturisers are important for improving the condition of the skin.

Topical corticosteroids are the main drug treatment. The choice of corticosteroid depends largely on the site of the atopic dermatitis.

Topical calcineurin inhibitors can be considered for sensitive sites such as the face where potent topical corticosteroids are potentially harmful.

Adjunctive treatments given during flares of dermatitis include bleach baths and wet dressings. Antihistamines may help to relieve itch.

Phototherapy may be considered by a specialist for adults if there is inadequate response to treatment.

Severe cases of atopic dermatitis may require systemic treatment. Immunosuppressants, such as ciclosporin, have been used and now dupilumab and upadacitinib are available for severe chronic atopic dermatitis.

Introduction

Atopic dermatitis is a common, multifactorial skin condition that is often managed by GPs. It affects all ages and is heterogeneous in appearance. While there is usually a flexural predominance, it can be localised to the face or hands, or be generalised. Patients complain of itch as well as the rash.

Management of atopic dermatitis is similar in adults and children. It requires a combination of drug and non-drug therapy. Corticosteroids are the mainstay of drug therapy, but biological drugs are now available.

Non-drug treatment

The aim is to manage aggravating factors and improve the condition of the skin. All patients should be instructed to use soap substitutes or bath oils long term.

Avoiding triggers

It is usually possible to identify factors that trigger a flare of atopic dermatitis. Some triggers can be avoided.

Heat

Most patients report that their skin flares in response to heat. Hot baths or showers, bedding, warm clothing or exercise can all be triggers. Patients should be educated to avoid overheating and use cool compresses when their skin is hot or itchy.

Irritants

Soaps, detergents, rough fabrics, seams, clothing labels and exfoliants may all aggravate atopic dermatitis.

Allergens

Not all patients with atopic dermatitis have allergies, but allergens can play a role in some patients. Fragrance is the most common cause of contact allergy, followed by preservatives in consumer products, for example methylisothiazolinone. Patients should always use fragrance-free products. Do not use products containing essential oils (e.g. lavender oil), or food ingredients (e.g. oatmeal, goats' milk, nut oils, pawpaw); these have a high risk for causing sensitisation and consequent food allergy. Sensitisation to contact allergens is more common in atopic individuals due to their impaired skin barrier, but can also occur in those without a known history of atopy. Dietary restrictions are to be minimised, particularly in infants, without input from specialists. Animal dander, house dust mite,[1] pollens and grasses are other potential allergens to recognise

and avoid. Skin prick and RAST testing are of limited diagnostic yield in most cases of eczema.

Moisturiser

Moisturiser is the cornerstone of the management of atopic dermatitis. A genetic tendency to dry skin, caused by filaggrin mutations, underlies most cases. Keeping the skin well moisturised ensures the skin barrier remains intact, prevents penetration of pathogens and allergens, and minimises itch. Patients should moisturise at least daily, but more often if their skin is particularly dry, or during flares.

Moisturisers should be tailored to the sites affected and patient preference. For example, a greasy moisturiser containing liquid paraffin may be suitable around the mouth of a dribbly infant but on the face of an adolescent it may cause acne. Lighter moisturisers may be preferable for hairy areas where folliculitis is more common.

The latest advances in moisturisers specifically for atopic dermatitis include the addition of ceramides which help to repair the deficient skin barrier and restore water permeability.[2-5] Some also contain prebiotics and probiotics to assist in homeostasis of the skin flora and minimise the predominance of *Staphylococcus aureus*. These eczema-specific moisturisers should in theory be more efficacious than standard moisturisers, however it is usually acceptable for a patient to use any bland moisturiser rather than nothing at all.

Drug treatment

The goal of drug treatment is to clear the atopic dermatitis completely. Undertreatment is likely to lead to recurrence.

Topical corticosteroids

Topical corticosteroids are the most important pharmacotherapy for atopic dermatitis. However, the correct selections of strength, quantity and duration of use remain major problems for both GPs and patients alike.

Patients should be counselled that topical corticosteroids are effective and safe when used correctly and should not be avoided or used sparingly. One of the common reasons for treatment failure is underuse due to steroid phobia. Patients are often concerned about the risk of skin thinning, becoming reliant on a corticosteroid, or that corticosteroids make things worse in the long term. They should be counselled that if the correct strength is prescribed for the site, then there is unlikely to be any concern with using a corticosteroid until the skin is clear. This can take weeks to months depending on the severity and chronicity of the atopic dermatitis. Treatment can be repeated on and off, for years if necessary. There is no need to taper topical steroids. They can be stopped when the skin is clear, or reduced to twice a week as maintenance in recurrence-prone areas.

Face

Only the weakest topical corticosteroids, hydrocortisone 0.5% or 1%, are relatively safe on the face and eyelids. If they are effective, they can be used twice a day until the skin is clear. Higher potency topical corticosteroids should be avoided as they commonly cause periorificial dermatitis, a form of steroid-induced rosacea. Other adverse effects such as telangiectasia, acne and erythema can also occur when moderate- and high-potency topical corticosteroids are applied to the face for prolonged periods. Cataracts and glaucoma are the main risks of long-term use of potent topical corticosteroids on the eyelids. If hydrocortisone is ineffective after two to four weeks, then non-steroid options such as a calcineurin inhibitor, or crisaborole should be considered.

Body and limbs

The body and limbs are more tolerant of topical corticosteroids than the face, with few adverse effects. Patients should be reassured that skin thinning is rare and, if seen, reversible. Suitable strengths include methylprednisolone aceponate 0.1%, or mometasone furoate 0.1%. These are used once daily until the skin is clear, then as needed. Ensure patients have a prescription for at least one to two months supply. An authority prescription may be needed to obtain adequate supply through the Pharmaceutical Benefits Scheme (PBS).

Hands and feet

The thick skin of the palms and soles requires a high-potency topical corticosteroid to achieve clearance of atopic dermatitis. Betamethasone dipropionate 0.05% is the standard strength for these sites. Apply twice a day until clear. These sites take longer to clear than other areas – four weeks is usual.

Calcineurin inhibitors

Pimecrolimus and tacrolimus are useful topical anti-inflammatory drugs for the treatment of atopic dermatitis. They are particularly used on the face and eyelids when mild topical corticosteroids are ineffective and where potent topical corticosteroids are not desirable.

Pimecrolimus 1% cream is available on the PBS (authority prescription) for specified patients over six months of age. It is used twice daily until the skin is clear. It can then be reduced to twice a week as maintenance therapy.

Tacrolimus is only available in Australia on a private prescription, compounded as either

cream or ointment in strengths of 0.03% or 0.1%. Tacrolimus 0.03% is equivalent to pimecrolimus 1%.

The main adverse effect of calcineurin inhibitors is a stinging or burning sensation on initial use. This normally subsides after a few days and is not harmful. Discomfort can be minimised by keeping the drug in the fridge and applying moisturiser first.

Crisaborole

Crisaborole 2% cream is approved for mild to moderate atopic dermatitis in patients over the age of two years. It is a phosphodiesterase-4 inhibitor which works by reducing cytokines including tumour necrosis factor alpha.

In clinical trials, 30% of patients were clear or almost clear after 28 days of crisaborole, compared to 18–25% with placebo (vehicle-only).[6] There are no trials comparing its efficacy to topical corticosteroids. The main adverse effect of crisaborole is stinging (4%), followed by flare of atopic dermatitis, pain and skin infection. Apart from the limited efficacy of crisaborole for atopic dermatitis, cost may limit use, with 60 g crisaborole costing approximately $145 on private prescription.

Adjunctive treatments

Bleach baths, oral antihistamines and wet dressings are all potentially helpful adjunctive therapies when patients have a flare of atopic dermatitis. See Box for useful resources that include patient handouts and videos.

Bleach baths

Patients with broken skin, weeping, crusting or sores should be instructed to have bleach baths. Plain, fragrance-free household bleach is added to the bath (¼ cup (62.5 mL) to a child's half-full bath, ½ cup (125 mL) to a full adult bath) for two to five minutes before getting out and patting dry. Oral antibiotics are generally not required unless the patient is systemically unwell or has failed to respond to bleach baths.

Antihistamines

Antihistamines can provide some relief from itch when given regularly. Less-sedating drugs, for example cetirizine or loratadine, are given during the day. Sedating antihistamines, for example promethazine or cyproheptadine, are given at night if sleep disturbance is a problem. Sedating antihistamines should not be used in children under the age of two years. Less-sedating antihistamines are considered to be relatively safe from the age of six months.

Wet dressings

Soaked clothing, tubular bandages or cloths held in place with crepe bandages can be used overnight or for periods of around four hours. They give relief from itch and aid penetration of moisturiser and topical corticosteroids.

Second-line treatments

Patients should be reviewed several weeks after having a flare of atopic dermatitis to check for response to treatment. If there is no response or response is inadequate based on skin appearance, symptoms of itch, poor sleep, or impact on school, work, family functioning or mental health, then further treatment and specialist referral are required.

Oral prednisolone has been used to treat flares of atopic dermatitis. While this may result in short-term improvement, many patients will require recurrent courses of prednisolone due to the long-term genetic tendency to atopic dermatitis. However, prednisolone, rather than topical corticosteroids, is the source of corticosteroid adverse effects, and it should be avoided if possible. There are safer, more effective options than prednisolone to consider in patients requiring more than topical corticosteroid treatment.

Phototherapy

Phototherapy with narrowband ultraviolet B (UVB) results in significant improvement in most patients with atopic dermatitis. A history of exacerbation with sun exposure, melanoma, or very fair skin (skin phototype 1) are contraindications. Lack of access to services in rural areas and not being able to attend due to work commitments are barriers to treatment. Phototherapy is generally not administered to children until they are able to comply with safety measures such as wearing goggles and standing unaided in the light cabinet.[7]

Immunosuppression

Ciclosporin is PBS-listed for treating severe atopic dermatitis. This is a medium-term treatment option (up to two years) due to the significant risk of renal impairment, hypertension and the potential for serious infections.

Drugs that have been used off label for atopic dermatitis include methotrexate, mycophenolate mofetil and azathioprine. Immunosuppressive drugs have largely been superseded by newer advanced therapies.

Box **Useful resources for adjunctive treatment**

Eczema. Kids Health Information Fact sheet. Royal Children's Hospital Melbourne.

Formula for an eczema bath. Royal Children's Hospital Melbourne.

Eczema wet-dressings video. Sydney Children's Hospitals Network.

Dupilumab

Dupilumab is a monoclonal antibody that blocks the binding of interleukins 4 and 13, which are key drivers of atopic dermatitis. It is an immunomodulator, not an immunosuppressant.

Dupilumab must be prescribed by a dermatologist or immunologist and is given as a fortnightly subcutaneous injection, for indefinite use. It is administered in conjunction with topical treatments.

The key trials of dupilumab report that two-thirds of patients will achieve a greater than 75% reduction in severity by 16 weeks and this is maintained out to 52 weeks.[8] Registry data suggest that real-world experience is in fact better than this, with 70–89% of patients achieving 75% skin clearance by week 52.[9,10]

Patients treated with dupilumab should use lubricant eye drops to avoid conjunctivitis, which is seen in around one-third of patients. They may complain of red, itchy, watery or gritty eyes. This is usually allergic conjunctivitis, or blepharitis, which can be exacerbated by dupilumab. It is generally mild to moderate and temporary. General practitioners should advise patients to increase the frequency of lubricant eye drops, add in topical and oral antihistamines, and treat their eyelids with tacrolimus ointment. A referral to an ophthalmologist may be required if symptoms persist.

Dupilumab is PBS-listed for severe chronic atopic dermatitis with an Eczema Area and Severity Index (EASI score) of 20 or more, or severe involvement of the hands or face. Patients currently must be aged 12 years or older (although it has recently been approved by the Therapeutic Goods Administration for children aged 6–12 years with expected PBS listing to follow) and have failed four weeks of appropriate topical corticosteroids or calcineurin inhibitor therapy.

Upadacitinib

Upadacitinib is a selective Janus kinase 1 (JAK 1) inhibitor, which blocks downstream signalling of multiple cytokines. It is therefore immunosuppressive. Oral upadacitinib has a rapid onset of action, with 70–80% of patients achieving 75% reduction in the severity of atopic dermatitis by 16 weeks.[11]

JAK inhibitors can cause cytopenias and elevation of lipid levels, so blood-test monitoring is required. The most common adverse effect of upadacitinib is acne. Infections, particularly herpes simplex and zoster, are also increased. Patients with suspected infections should be assessed and managed promptly. Consider empiric antiviral drugs if zoster or herpes simplex is suspected. The patients should be advised to withhold upadacitinib until they have fully recovered.

Patients should be fully vaccinated before starting treatment. Live vaccines are contraindicated during treatment.

The PBS criteria for upadacitinib are the same as for dupilumab.

Conclusion

The management of atopic dermatitis combines drug and non-drug therapy. Topical corticosteroids are still the main drug treatment, but other options, such as topical calcineurin inhibitors, may be used at some sites. Immunomodulating and immunosuppressive drugs may be required for severe cases of atopic dermatitis. ◀

Conflicts of interest: Gayle Ross has been a paid speaker and on medical advisory boards for Abbvie, Leo Pharma, Sanofi Genzyme, Lilly, Johnson & Johnson and Ego Pharmaceuticals.

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