Management of atopic dermatitis – A review

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Abstract
Atopic dermatitis is a chronic relapsing and remitting disease, which afflicts mostly the young ones. The treatment of atopic dermatitis is very frustrating as no single therapeutic modality is satisfactory. The first breakthrough in its management came with the advent of topical steroids. We are still awaiting the next breakthrough. Much research is being done in this regard and the pick of the lot is topical immunotherapy. It may well prove to be the find of the decade in the management of atopic dermatitis. This article summarizes the established as well as unconventional therapeutic modalities which help the patients as well as which has evidence of successful use.

Key words
Atopic dermatitis, management

Introduction
Atopic dermatitis is a chronic relapsing and remitting disorder, which usually starts in early childhood. It is frequently associated with elevated levels of serum IgE and a personal or family history of atopy i.e. allergic rhinitis, atopic dermatitis or asthma. The diagnosis is clinical and based on a combination of historic and morphologic finding, as there is no single distinguishing feature.1 Atopic dermatitis now affects 15% to 20% of children in developed countries, and prevalence in cities in developing countries undergoing rapid demographic changes is quickly following suit.2 The condition also creates a great financial burden for both the family and society.3

General measures
Perhaps the most important consideration in the management of atopic dermatitis is to educate the patient and family in certain realities of their disease.
1. The disease runs its own course and physicians can only moderate that course; the disorder is not curable but it is always possible to improve the patients' condition.
2. The skin must be kept moisturized.
3. It is crucial that trigger factors are avoided in order to prevent inflammation.

a. Mild cleansing
Routine everyday care of skin is an essential part of optimal patient management in atopic dermatitis. Xerosis, which is an integral part of atopic dermatitis, leaves the skin vulnerable to external insults, partly as a result of varying levels of barrier dysfunction. Cleansing removes dead surface cells, preparing skin to better absorb topically applied drugs/medication. Cleansers based on mild synthetic surfactants and/or emollients are ideal for these patients.4

b. Emollients
Emollients and moisturizing creams are used to break the dry skin cycle and to maintain the smoothness of the skin. In the
vast majority of cases, improved bathing techniques and proper moisturizing can solve the problem. Patients need to avoid hot water, overuse of soap and unnecessary soaking and rubbing with washcloth and towel. Excessive frequency of bathing and hand washing should be discouraged. Most importantly, the skin hydration obtained from bathing should be retained by prompt application of an adequate moisturizer. The least expensive moisturizers are mineral oil and petrolatum etc. Moisturizers should be applied lightly after the bath and any excess removed with a cotton towel. Creams and lotions may be irritating and drying due to an evaporative effect. Greasy agents should be avoided in hot humid climate to prevent occlusive folliculitis. Similarly plastic wrap occlusion may also cause folliculitis. Recently it has been shown that ceramide deficiency is the putative cause of stratum corneum dysfunction. Ceramide-dominant, barrier repair emollient has been shown to be better than simple emollients.

Established therapies

a. Antihistamines
Oral antihistamines provide only marginal antipruritic benefit and much of the effect seems to be as a sleep aid. Doxepin is the most potent histamine antagonist and is very specific. So is hydroxyzine, which is one of the few shown to be effective in a controlled trial. However, relief of pruritus by non-sedating antihistamines has been refuted. Several studies demonstrate the efficacy of second and third generation anti histamines in relieving pruritus in atopic dermatitis, but double-blind placebo-controlled trial are lacking. Cetrizine, a second generation antihistamine, has been shown to possess anti-inflammatory properties, acting via inhibition of leucocyte recruitment and activation, and by the reduction of ICAM-1 expression on keratinocytes.

b. Topical steroids
Topical corticosteroids have been the mainstay of treatment for atopic dermatitis over the past 40 years. Hydrocortisone was the first to be used; some 30 additional corticosteroid compounds have now been licensed for treatment of atopic dermatitis. Topical applications containing corticosteroid compounds vary greatly in potency. In general the more potent ones are associated with the greater risk of adverse effects. First application of potent topical steroids results in rapid clearance of the rash. The snag is that persistent application of a potent preparation will put the patient at risk of unwanted local effects on the skin. The development of side effects is directly proportional to the frequency of application of topical steroids. However, recent trials suggest that only once daily application can give optimal results, and maintenance treatment can be done effectively with only twice weekly application thus minimizing the side effects.

c. UVA therapy
Several studies have demonstrated the efficacy of UVA1 (340-400 nm) phototherapy for patients with severe atopic dermatitis. However, the optimum treatment dose has yet to be determined. Although in seminal investigations high UVA1 doses were used, comparable results were reported in recent studies with a medium-dose regimen. However, effectiveness is merely short term, limited, and is followed by recurrence of symptoms within a 3-month observation interval.
d. **UVB therapy**
Recently, interest has been renewed in the narrow-band wavelength of UVB phototherapy for atopic dermatitis (TL-01 Lamp). Encouraging results have been reported. However, long-term follow-ups are required before this therapeutic modality is established as treatment of atopic dermatitis.\(^{15,16}\)

e. **Antibacterials**
Secondary bacterial infections are known to complicate atopic dermatitis, due to deranged skin barrier function and impaired immunological status. *Staphylococcus aureus* is the infecting organism in over 99% of episodes. It is nearly always penicillin-resistant. Cloxacillin and erythromycin are reasonable choices of treatment. Recent research has greatly contributed to our understanding of the pathophysiological potential of *S. aureus* superantigens in atopic dermatitis, suggesting that antibiotic therapy might be an important element in the therapeutic management of atopic dermatitis.\(^{17}\)

**Newer modalities**

a. **Cyclosporin**
Oral cyclosporin is now an established therapeutic modality in severe and recalcitrant atopic dermatitis. Several studies have shown that short-term treatment is effective and tolerable as the drug is tapered off before side effects set in. Dosage regimen of 3-5 mg/kg/day for 10 to 12 weeks is effective.\(^{18,19,20}\)

b. **Topical macrolactum immunomodulators**
The immunomodulatory macrolactams provide an alternative to glucocorticosteroids for the topical treatment of atopic dermatitis and other inflammatory dermatoses. Tacrolimus (FK506), as well as the newer ascomycin derivative ASM 981 (pimecrolimus), penetrate the inflamed epidermis and are suitable for topical therapy. Both substances inhibit the transcription of proinflammatory cytokine genes such as interleukin 2, which are dependent on the nuclear factor NF-AT. They block the catalytic function of calcineurin, which leads to the inhibition of the transport of the cytoplasmic component of NF-AT to the cell nucleus. Multicenter, randomized, double blind clinical trials with topical formulations have shown the efficacy of both substances in moderate to severe atopic dermatitis.\(^{21,22}\)

c. **Montelukast**
Cysteinyl leukotrienes have been shown to be important in the pathogenesis of allergen-induced (atopic) asthma and rhinitis. Skin manifestations of atopic dermatitis have been reported to improve with leukotriene antagonists. Double-blind placebo-controlled trials have shown moderate response to montelukast in severe atopic dermatitis.\(^{23,24,25}\)

d. **Photopheresis**
Recently, photopheresis was used as monotherapy in patients with intractable atopic dermatitis. A total of ten treatments were used with a two weekly interval. All patients showed clinical improvement as well as reduction in serum levels of eosinophil cationic proteins and total IgE.\(^{26}\)

**Experimental modalities**

a. **Antifungals**
As fungal colonization is increased in atopic dermatitis, there is a rationale to use antifungals. Clinical improvement and decreased serum IgE were obtained in patients with positive *Malassezia*
radioallergosorbent tests (RASTs), who were treated with oral ketoconazole. Some preliminary data suggested that oral itraconazole treatment in AD patients reduced the need for topical corticosteroids. Furthermore, besides its antifungal action, itraconazole in part relieves pruritus and inflammation.²⁷

d. Balneotherapy
Balneotherapy involves immersion of the patient in mineral water baths or pools. Bathing in water with a high salt concentration is safe, effective, and pleasant for healing and recovery. There are almost no side effects during and after treatment, and there is a very low risk to the patient's general health and well-being. The mechanisms by which broad spectrums of diseases are alleviated by spa therapy have not been fully elucidated.²⁸ Such therapies are being used in many parts of Pakistan since ancient times. Many places are known for their hot springs and people travel from great distances to bathe in these waters.

c. Dinitrochlorobenzene
A small uncontrolled pilot trial has suggested that contact sensitization to dinitrochlorobenzene and repeated weekly applications significantly improve the clinical status of severe atopic dermatitis in adults. The effects are thought to be due to topical immune modulation by dinitrochlorobenzene. Larger controlled studies of dinitrochlorobenzene treatment in atopic dermatitis are warranted.²⁹

d. Intradermal Mycobacterium suspension
Recently a small randomized, double blind and placebo controlled trial has shown improvement in childhood atopic dermatitis using intradermal injection of killed Mycobacterium vaccae (SRL 172).³⁰

e. Naphthalan
Naphthalan has long been known for its medicinal properties and beneficial effects in inflammatory diseases such as psoriasis, atopic dermatitis, and psoriatic dermatitis. Experience acquired to date in the use of naphthalan in the management of squamous dermatoses and atopic dermatitis has shown favorable results. It should be further investigated to confirm its usage in the treatment of these diseases.³¹

f. Probiotics
Recent studies suggest that oral bacteriotherapy with probiotics might be useful in the management of atopic dermatitis. Lactobacillus GG (ATCC 53103), which is a human intestinal strain, promotes local antigen-specific immune responses (particularly in the IgA class), prevents permeability defects, and confers controlled antigen absorption, when given to infants with atopic eczema and cow's milk allergy as an extensively hydrolyzed whey formula containing (5 × 10⁸ colonyforming units/gm formula). Thereby it promotes endogenous barrier mechanisms in patients with atopic dermatitis and food allergy by alleviating intestinal inflammation.³²-³⁴

g. Interferon gamma
Recombinant human interferon gamma has been shown in a double-blind, placebo-controlled study to be a well-tolerated and effective agent in the long-term therapy of patients with AD, when given in a dose of 50 µg/m² as daily self-administered subcutaneous injection for up to 24 months.³⁵

h. Mycophenolate mofetil
Mycophenolate mofetil is a new immunosuppressive drug that is used to prevent acute rejection of renal
transplants. In doses of 2 or 3 g/d the drug is well tolerated, effective and safe in non responding atopic dermatitis.  

Complementary and alternative medicine

a. Acupuncture
Acupuncture is an old therapeutic method that includes both needle and non-needle acupuncture. Non-needle acupuncture includes moxibustion, cupping, and acupressure. Acupuncture has been reported to be beneficial for the treatment of atopic dermatitis among many other skin conditions. A lack of controlled studies is the main drawback for this method of treatment. However, the experiences from experts in this field may offer us new ideas to resolve refractory disorders in dermatology.

b. Traditional Chinese medicine
Traditional Chinese medicine (TCM) is an alternative method of therapy that can be administered in oral, topical, or injectable forms. It emphasizes the importance of using many herbs that are combined in different formulations for each individual patient. In the future, perhaps a better understanding of TCM will be gained through more systematic analysis and controlled studies with a placebo arm.

c. Homeopathic treatment
Homeopathy is one of the commonest alternative methods of treatment being used these days by dermatologic patients. Conflicting results of this treatment modality have been reported. Randomized, blinded and placebo-controlled trials are lacking in literature. Maybe a few good trials can settle this issue.

d. Special silk fabric
As it is well known, irritant factors aggravate childhood atopic dermatitis. A special silk fabric (MICROAIR Dermasilk) has been developed to minimize such irritant reactions. It has been shown that wearing such fabric minimizes symptoms in atopic children.

e. St. John's wort cream
Recent investigations suggest an anti-inflammatory and antibacterial effect of hyperforin, which is a major constituent of Hypericum perforatum L. (Saint John's wort). A double-blind, placebo-controlled prospective study has shown a significant superiority of the hyperforin 1.5% cream compared to the vehicle in the topical treatment of mild to moderate atopic dermatitis. The therapeutic efficacy of the hypericum-cream, however, has to be evaluated in further studies with larger patient cohorts, in comparison to therapeutic standards i.e. glucocorticoids.

f. Hypnosis
Hypnosis is an alternative or complementary therapy that has been used since ancient times to treat medical and dermatologic problems. A wide spectrum of dermatologic disorders may be improved or cured using hypnosis as an alternative or complementary therapy, including atopic dermatitis.

g. Oolong tea
Standard treatment fails in many patients with recalcitrant AD skin lesions. Study results in animal models have demonstrated that the administration of tea (i.e. green, black, or oolong) suppressed type I and type IV allergic reactions. This hypothesis has been tested clinically in an open study and oolong tea has been found to be effective in atopic dermatitis, probably due to antiallergic properties of tea polyphenols.
h. Natural honey and beeswax
A mixture of honey, olive oil and beeswax, all in equal proportions, applied topically, has been tested in a single blind, partially controlled study and found to be effective in the treatment of atopic dermatitis and psoriasis.46

Future
The fact that so many new, exotic and alternative treatment modalities are being sought, shows the amount of research being done in the field of atopic dermatitis, on the other hand it also shows the failure of medical science to discover a cure for this debilitating condition. Many other therapies (may be too exotic) could not be included in this article due to space constraint. However, the clinch of the recent research in the field of atopic dermatitis is the development of topical immunotherapy. Tacrolimus and pimecrolimus are, maybe the therapeutic finds of this decade in the treatment of atopic dermatitis.47 The very concept of applying topical steroids with all the long-term ill effects will be changed. But till the time these topical immunomodulators become widely available, and also at lower cost, the mainstay of treatment remains emollients and topical steroids.

References
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