



Atopic dermatitis and the therapeutic methods: a literature review

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ABSTRACT

Atopic dermatitis is an inflammatory skin disease that starts in the early life and usually persists by the end of life in 20% of cases. The disease shows multiple periods of relapse, and significantly affects the patient's quality of life. The etiology of this disease is unknown, yet recent studies have reported incidence of immunological disorders and mutation in the filaggrin gene as the major causes. In some cases, concurrent incidence of infection with these inflammatory lesions reinforces the significance of treatment. Various methods of treatment such as emollients, corticosteroids, and calcineurin inhibitors are applied to manage this disorder. Traditional and complementary approaches may also help to control the disease. This disease is not usually easily controllable, thus requires full awareness of physicians on the underlying prospects of this disease. This review paper deals with the important aspects of the clinical perspectives and presents an integrative therapeutic approach for treating atopic dermatitis.

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Introduction

Atopic dermatitis is an inflammatory skin disease that mostly occurs in children. The meaning of the word "Atopy" is the affinity to secrete immunoglobulin E (IgE) against environmental allergens. Dermatitis signifies inflammation in the skin. Typically, the terms dermatitis and eczema are used interchangeably, while the word eczema often represents the acute manifestations of this disease. However, in this review there is no difference between these two terms. Allergic sensitivity and increased IgE levels occur in half of patients; therefore, the word atopic dermatitis does not always apply literally (1,2). Since atopic dermatitis

is a long term and annoying disease, in the present article we decided to review various methods of treatment of this disease.

Literature review

1. Epidemiology

Atopic dermatitis has a variable prevalence around the world and around one fifth of people are affected by this disease during their life. In industrial countries, prevalence of this disease has grown in 19th century due to development of allergens in the environment. However, current studies show that this disease has declined dra-

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matically in countries with a high previous prevalence such as England. This suggests reduction of allergens in the environment over time. Nevertheless, this disease is still regarded as a major health problem especially in developing countries (1). Around 50% of people suffering from this disease experience the outset of symptoms in their first year of life, while about 95% experienced it when they are less than five years of age (2). In approximately 70% of individuals, relapse of this disease takes place before puberty, whereas 25% of individuals experience the symptoms and relapse of this disease even after puberty. Around 60% of children that are inflicted with this disease at the beginning of the birth are sensitive to one or several allergens, while the children experiencing late onset of this disease are often less sensitive (3). Although many patients are sensitive to allergic foods or allergens present in the air, these allergens rarely cause aggravation of the symptoms of this disease. Sometimes these factors intensify the risk of incidence of other atopic diseases including asthma (4).

2. Risk factors

The disease risk of incidence is higher in people with familial background. Genetic factors play an important role in susceptibility of a patient to atopic dermatitis (5). On the other hand, environmental factors definitely play some roles. Therefore, it can be deduced that this disease is a genetic or genetic-environmental disease (6,7). Although the risk of many environmental factors has been expressed as the causes of this disease, only a few of them have been accepted. For example, Western lifestyle has been considered an important risk factor over the recent years (8). In addition, the hypothesis of hygiene is another risk factor that has resulted in intensified incidence of eczema (9). This hypothesis signifies that the probability of incidence of eczema is lower in individuals, who had been subjected to infectious diseases such as hepatitis in their childhood (10-12).

3. Pathophysiology

Two hypotheses are introduced to explain the occurrence of inflammatory lesions in atopic dermatitis. The first one suggests that this disease is the results of imbalance of T-cells especially T helpers of 1, 2, 17, and 22 types as well as regulatory T cells. In this disease, particularly in acute eczema, CD4+ T cells are differentiated into Th2, resulting in increased production of interleukins (IL). At the first stage, IL-4, IL-5, and IL-13 are increased, followed by elevation of IgE levels. Differentiation of Th1 cells is inhibited in this process (13,14).

The second hypothesis that has been propounded

is related to destruction of skin barrier. This hypothesis has been recently put forward and states that individuals, whose filaggrin gene has undergone mutation, are at a high risk to develop this disease (6). The filaggrin gene encodes the structural proteins of Stratum corneum. In addition, this gene encodes the proteins associated with stratum granulosum, which help connecting keratinocytes to each other. All these factors join together and bring about the development of skin barrier and its humidification. Therefore, any defect in this gene causes disruptions in the structure of skin barrier. This means that the skin becomes dry, its permeability to allergens increases, and finally the signs of eczema emerge (15).

4. Diagnosis and clinical presentations

The skin morphology of atopic dermatitis lesions is approximately the same as other eczemas. This disease, in its acute form, emerges as red and pustular split vesicular lesions. In acute and chronic states, these lesions change into papule and nodule lesions. In addition to these signs, diagnosis is also made based on other properties including the region of eczema distribution and familial background of the patient (16,17). In general, the typical characteristic of patients affected by atopic dermatitis is the presence of itchy lesions at certain sites such as curved and folded points (18,19).

The clinical manifestations of eczema are usually accompanied by wide changes in the morphology and the distribution area of the eczema and other factors. In general, most of patients with eczema have a dry skin with very low water content. They have a pale skin with no ability to perspire. When a trivial scratch occurs, an extreme cholinergic response is developed, where the soles and palms become hyperlineated. The hair of these patients is dry and brittle. The region around their eyes becomes dark due to hyperpigmentation following an inflammation.

In addition to above-described typical manifestations, other common and mild dermatological signs are also exhibited in some patients. For example, pityriasis alba, in which dry and pale spots appear on the face and upper part of the arm, or keratosis pilaris that emerges in the form of hard and small keratolytic papules especially in the upper parts of the arm and thighs. Many patients are sensitive to wool clothes, resulting in intensified scratching. Hot and long water bath should also be avoided in these patients. The majority of infections including staphylococci are the main causes of disease aggravation. Many diseases cause skin rashes, which are similar to the atopic dermatitis. However, through carefully examining the morphology and localization site

of the lesions and by gaining information of the patients themselves, this disease can be differentiated from diseases with similar symptoms. For example, contact dermatitis most of the time has a similar appearance to atopic dermatitis (16,17).

5. Complication

Many microorganisms (bacteria, viruses, and fungi) can contribute to exacerbation of the eczema lesions. The skin of people affected by this disease has often been colonized by *Staphylococcus aureus*, especially when eczema has not been controlled well. The mere presence of these bacteria does not necessitate the use of antibiotics. Nevertheless, if this staphylococcal infection becomes aggressive (impetigo), topical or preferably oral antibiotics should be used. Usage of anti-infective solutions such as Chlorhexidine can decrease microbial load, yet it can result in sensitivity (20).

6. Treatment

Atopic dermatitis is known as a chronic disease and usually it cannot be cured completely. Therefore, the only therapeutic approaches for the treatment of this disease are considered as follow: 1) Reducing the frequency of disease flares. This aim is indeed the same as prevention. 2) Curtailing the duration and intensity of the flares. By this aim, treatment is meant. Prevention is usually met by mitigating dryness of the skin through moisturizer or emollient creams. When skin dryness is solved, the probability of itching and thereby development of infection declines. Use of emollients after taking bath also leads to preservation of epidermis moisture, thus improving the performance of skin barrier. When eczema is aggravated, application of drug treatments is needed, for which corticosteroid creams are usually employed. In acute and chronic eczema, in addition to topical treatments, systemic immunosuppressant drugs or (UV light) phototherapy are required (21-23).

6.1) Emollients

These substances help in preserving the skin barrier. They should be used several times a day, resulting in decreased need to topical corticosteroids. The reason of using emollients is their ability in increasing the water transfer to epidermis. The main mechanism of action of these substances is prevention of water evaporation through developing an occlusive layer in the upper part of the skin. Therefore, emollients do not have a direct effect on the eczema itself. Application of these substances causes the skin to appear better and the scratches to diminish. Some moisturizers have a more complex performance, where they can contribute to

repairing the lipid components of the structure of skin external layers, thus reducing the gaps within the skin. Other groups of these substances are also available that can help in preservation of the moisture of the skin through absorbing water molecules from the air on the skin. Moisturizers are selected based on the skin characteristics of individuals. The moisturizers with high lipid content like ointments are recommended in dry skins whereas semisolid bases with low lipid or high water content are administered for mild cases. Due to their rapid absorption, such creams should be used multiple times a day. It is better that emollients with no odor or other allergens are used to prevent the secondary sensitizations (22).

6.2) Topical corticosteroids

Topical corticosteroids, whether in children or adults, are the mainstream treatment of moderate to severe atopic dermatitis. This medication groups are classified into four classes (mild, moderate, potent, and very potent) based on their vasoconstrictory properties. The most potent corticosteroid is clobetasol and the least potent one is hydrocortisone. Many patients are treated with mild to moderate corticosteroids. A small group of patients need potent products in severe cases of the disease. Very potent products are seldom required. Mild to moderate corticosteroids are used for children, while adults are treated with more potent products. Mild to moderate corticosteroids should be mainly utilized in the treatment of eczema in parts of the body with thin skin such as face, groins, or genitalia, while more potent types are reserved for other parts of the body like hands. Typically, patients and physicians are less inclined to administer these medications due to their side effects. The untoward effects of topical corticosteroids are skin thinning and stretch marks, though if they are used properly, fewer side effects emerge (24).

6.3) Calcineurin inhibitor

The topical dosage form of calcineurin inhibitors (tacrolimus, pimecrolimus) are mainly used in maintenance therapy of this disease. Pimecrolimus has a potency equivalent to that of the mild corticosteroids, whereas tacrolimus can be equaled with moderate to potent corticosteroids. The side effects of corticosteroids are not observed in this drug group thus can be used daily in long term treatments (25).

6.4) Phototherapy

Disseminated eczema is usually treated with UV light. Narrow band UVB light is utilized in the treatment of adult resistant eczema. UVA light with a wider band or a combination of UVA and psoralene

light-sensitizer drug are used in the treatment of highly more severe eczema. This therapeutic approach causes skin aging and increased susceptibility to skin cancer in the long term (22,23).

6.5) Systemic immunosuppressants

In the treatment of disseminated and severe eczema, a short period of oral corticosteroids is recommended. Topical corticosteroids are also used in conjunction with the oral ones. Due to the presence of some infections that lead to relapse of signs and their aggravation, taking oral antibiotics is also essential. Owing to the side effects of corticosteroids, continuation of the oral regimen is not usually recommended, and thus these medications should be tapered off (26).

6.6) Acupuncture

EX-HN3, LI4, LI11, TE5, ST36, SP6 and LR3 are the acupuncture points on both sides of the body. Some special points of acupuncture were also identified for atopic dermatitis (EX-HN3, LI4, LI11, TE5, ST36, SP6 and LR3 on both sides of the body). Acupuncture needles were inserted subcutaneously and they are kept for about 15 min. During the treatment course, this method should be applied twice a day (27).

6.7) Phytotherapy

Decoction formulation of different plants such as *Glycyrrhiza glabra*, *Plantago asiatica* L., *Rehmannia glutinosa*, *Atractylodes chinensis* and *Raphanus sativus* are used to decrease the erythema, secretions, and itching caused by this disease. Around 0 to 20 g of each plant is decocted with pure water. This amount is the daily dosage of the patient, which should be taken by the patient on three occasions after each meal. This formulation does not have any hepatotoxicity or nephrotoxicity. The antibacterial properties of phelodeni cortex have also been identified. Three to four layers of gases impregnated with the decoction formulation of this plant are placed on the lesions of the disease, once or twice a day, for 20 to 30 min, thus mitigating the signs (27).

6.8) Probiotic therapy

The effectiveness of probiotics in allergic diseases like eczema has been mentioned in different studies. The researchers believe that the results are promising, but more studies are necessary to confirm their definitive role. For instance, *Lactobacillus* was administered to pregnant women who suffered from eczema and to their infants up to the age of 6 months. As a result, the likelihood of atopic dermatitis occurrence in children was dramatically reduced at 2 and 4 years. Probiotic ther-

apy is very effective in children with high IgE levels and the children who showed one or more positive skin tests. The results of a controlled clinical trial demonstrated that *Lactobacillus* can be very effective in children who simultaneously suffer from atopic eczema and allergy to cow's milk (28). Several mechanisms have been proposed for the effects of probiotics, most notably including: regulating the immune system, showing antimicrobial effects, blocking inflammation and stopping the death of epithelial cells by secreted proteins and DNA as products of probiotics (29).

Conclusion

Atopic dermatitis is a disease that affects people from childhood and continues for a long term. Not only its annoying complications, but also sometimes the associated infections, necessitate different methods of treatment. In this review, several therapeutic strategies upon integrative medicine are introduced to provide the possibility to choose the desired treatment based on patient status including age, sex, lesion region and drug safety.

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Conflict of Interest

The authors declare no conflict of interest.

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