

REVIEW ARTICLE

Relationship Between Atopic Dermatitis and Food Allergy

Olga Domínguez^{1,*}, Ana María Plaza¹, Montserrat Alvaro¹

¹Department of Allergy and Clinical Immunology, Hospital Sant Joan de Déu, Barcelona, Spain

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Abstract: Consistent evidence has been found on the relationship between food allergy (FA) and atopic dermatitis (AD) in some children. Food sensitization can be often found in these patients. Allergy should be confirmed, though, with a food challenge test (FC) before advising a restrictive diet which could be harmful for the patient. Younger children with AD frequently show sensitization to egg, milk or peanut, while older ones and adults are more often sensitized to environmental allergens such as house dust mites, moulds, animal dander or pollens. It is well known that a barrier disturbance plays a main role in the development of sensitization and allergy. Therefore, due to the early appearance of AD, preventive newborn skincare with emollients and early introduction of food appear to be very important to determine food tolerance.

Keywords: Atopic dermatitis, food allergy, oral food challenge, food sensitization, food-triggered atopic dermatitis.

1. INTRODUCTION

Atopic dermatitis AD is the most common chronic inflammatory skin disease in children. The etiology is multifactorial and its appearance shows characteristic erythema, wounds, dry skin and intense itching. Its prevalence in children is continuously increasing with rates ranging from 5 to 20% of pediatric population. FA is also rapidly increasing. Cipriani [1] reported, in an American national study, the total prevalence of 13 % of AD in children, with 67% being mild, 26% moderate and 7 % severe. However, there is a lower prevalence in less developed countries. Nevertheless, a multinational study of AD prevalence [2] in children aged 12-15 months showed a variation with a range of 10.6% in Valencia (Spain) to 28.2% in Honduras. The average prevalence was lower in Europe (14.2%) than in Central America; therefore increasing also in less developed countries.

Forty-five percent (45%) of the subjects start experiencing symptoms before the age of 6 months. Gramhausen [3] reported different patterns of evolution after an examination of 725 teenagers and adults. The most common pattern shows the beginning of symptoms before the age of 2 years lasting further than the age 20. Other patterns have also been found: start of symptoms after age 20 (18%), between 2-6 years (13 %), between 6-14 years (9.5%) and between 14-20 years (12.6%), all three lasting further than age 20 and showing a decreased severity in all of them when they grow older.

2. RISK FACTORS AND ASSOCIATIONS

About 70% of AD patients have a family history of atopic diseases. The odds ratio for the development of AD is

2-3 times higher in children with 1 atopic parent, and 3-5 times higher in children with 2 atopic parents. A maternal history of AD may be associated with a higher risk of developing AD [4].

Loss of function mutation in the filaggrin (FLG) gene: this gene encodes an epidermal structural protein. About 10% of the population of European ancestry has 1 null mutation in FLG, and they are reported to have 3 times higher likelihood of developing atopic dermatitis [5]. FLG null mutations may increase the risk of earlier onset and more severe persistent AD. However, FLG null mutations are absent in many patients with atopic dermatitis, and up to 60% of people with the mutation do not develop atopic dermatitis [6]. Other genetic risk factors include mutations in genes involved in epidermal barrier functions, environmental sensing, immune regulation and tissue response.

The reported environmental risk factors include: “western diet” (consisting of high amounts of sugar and polyunsaturated fatty acids), small family size, high education level, living in urban settings and living in regions with low exposure to ultraviolet radiation and low humidity [7].

These factors, in combination with genetic factors, will lead to a change in an immunological phenotype that could increase or decrease the possibilities of developing AD.

ISAAC study [8], which included 591 children between 8 to 12 years old in 20 countries, concluded that the association between allergic sensitization and AD was higher in developed countries and found a higher correlation between asthma prevalence and AD. This asthma had the worst prognosis. The severity of AD is a factor determining the subsequent development of allergic diseases.

The Canadian Healthy Infant Longitudinal Development Study [9] found that children with AD and allergic sensitiza-

*Address correspondence to this author at the Department of Allergy and Clinical Immunology, Hospital Sant Joan de Déu, Barcelona, Spain; E-mail: odominguez@sjdhospitalbarcelona.org

tion had a greatly increased risk of food allergy, asthma and allergic rhinitis compared to non-sensitized children without AD.

3. SKIN ROUTE OF SENSITIZATION TO FOODS

A genetic predisposition leads to a dysfunction of the skin barrier and subsequent inflammatory injury and immunological disturbance of TH2 cells. This causes the liberation of cytokines that maintain an inflammatory skin status. This dysfunction of the skin barrier enhances the entry of allergens and irritants which contributes to a loss of hydration and persistence of sub-clinic skin inflammation.

The paradigm of the inflammatory response in the skin after exposure to allergens involves epidermal antigen-presenting cells (dendritic cells and Langerhans cells) that express high-affinity IgE receptors, binding the antigen and presenting it to T cells, (mainly TH2) leading to local inflammation. Regulatory T cells and, more recently, regulatory B cells of various subtypes, have been described as playing a role in the pathogenesis of AD and FA as well as in the development of tolerance to the involved foods (10). Thus, one of the main immunological features in AD is the imbalance between Th1 / Th2.

With the acute status of AD, the allergen-activation of Th2 cells is prevalent to Th1, in affected as much as in healthy skin. In healthy skin, nevertheless, the production of INF- γ by Th1 cells is more prevalent.

Polymorphisms in Th2-related genes, in particular, have been associated with an increased risk of AD. IL-4 and IL-13, the most commonly involved cytokines, have been shown to contribute to epidermal barrier dysfunction, migration of inflammatory cells into AD lesions, innate immune suppression, and the characteristic pruritus in this condition. Currently, dupilumab (anti-IL-4R) is the only commercially available antibody inhibitor for AD.

The role of filaggrin mutation in food allergy has been demonstrated in a [11] study, which included 1184 patients in Manchester, with a follow-up involving different ages. They measured the content of peanut antigen in domestic dust in the early years of life. A sensitization study with skin prick test and immuno-Cap to Ara h 1,2, 3 and an oral exposition test to peanut was conducted. It was concluded that an environmental exposure to peanut at early ages is related to an increased sensitization and peanut allergy in children showing a mutation for filaggrin. This shows a trans-epidermal sensitization due to a skin barrier disturbance.

Lack [12] suggested the dual-allergen-exposure hypothesis which states, in one hand, that food tolerance is induced from the oral exposure to a food antigen, enhancing immune response to suppress allergy and, on the other, that infants with eczema are exposed to food antigen via skin inducing immune cells, producing IgE antibodies (sensitization) and promoting allergy. This hypothesis implies that it is important not only to induce oral immune tolerance, but also to prevent allergic sensitization through the skin in order to reduce allergies. Lack *et al.* [13] also demonstrated that peanut allergy was associated with the use of skincare products containing peanut oil in England. The results from the study

suggested that peanut allergens absorbed through the skin may cause allergic sensitization.

ALB/c mice were epicutaneously sensitized with repeated applications of ovalbumin to tape stripped skin over 7 weeks, or orally immunized with ovalbumin and cholera toxin over 8 weeks. Both the epicutaneous and orally exposed groups of mice demonstrated sIgE antibody responses, and yet only those without oral immunization had signs of anaphylaxis on oral challenge. Thus the determination of FA or tolerance depends not only on a period of cutaneous sensitization, but also on the timings and likely amount of gastrointestinal tract allergen exposure.

The role of IL-33 in mediating oral anaphylaxis through epicutaneous sensitization is also emerging. In another murine model of epicutaneous OVA-sensitization, the epithelial harm induces the release of IL-33, which enhances IgE-mediated mast cell degranulation leading to anaphylaxis after an oral antigen challenge.

The rise of trans-epidermal water loss (TEWL) two days after birth is also a predictor of allergy development at two years of age [14]. Neonatal skin barrier dysfunction predicts FA at 2 years of age, supporting the concept of transcutaneous allergen sensitization, even in infants who do not have AD. In a study, the relation between the barrier function and FA in children was studied. TEWL was measured in the neonatal period, at 2 and 6 months of life. Two years old children sensitized to food (positive skin prick test) underwent an oral food challenge (OFC). One thousand three hundred fifty-five (1355) children were evaluated at age 2 years, and 1260 underwent skin prick test and oral food challenge screening. Food sensitization was present in 6.27% and FA prevalence was 4.45%. The egg was the most prevalent allergen (2.94%), followed by peanut (1.75%) and cow's milk (0.74%).

Day 2 upper-quartile TEWL was a significant predictor of FA at age 2 years. Seventy-five percent of children with FA at 2 years of age had day 2 TEWL in the upper quartile [14].

S. aureus colonization, mainly methicilin-resistant (MRSA), is also associated with higher FA risk. Thus, microbial cutaneous dysbiosis also plays a role in barrier dysfunction modulating allergic sensitization [15].

All these evidence make repairing of the cutaneous barrier with an early treatment an important point to prevent sensitization and FA.

4. IS THERE A LINK BETWEEN AD AND FA?

It is known that children with AD are at a higher risk of FA, with up to a third of children with moderate to severe AD experiencing IgE-mediated food allergies [16]. A European cohort study [17] noted that both early transient and early persistent AD increased the risk of food allergy at aged 6 (aOR 3.69; 95% CI 1.93, 7.035, and aOR 7.08; 95% CI 3.59, 13.975, respectively).

In the HealthNuts study [18], 4000 children with AD were evaluated during their first year of life. They showed a risk of becoming peanut allergic and egg-allergic higher at 12 months of age.

In a systematic review [13] of AD and FA within 66 studies, it was shown that food sensitization was 6 times higher in children with AD compared to healthy controls at 3 months of age.

There have been 16 studies showing that FA is associated with a more severe FA phenotype and other 6 studies showed that early development and persistent AD are linked to FA. So it is known that there is a strong association between severe AD with early start, sensitization and FA [19-22].

Flohr *et al.*, (19) analyzed those undergoing SPTs at 3 months within the Enquiring About Tolerance (EAT) study UK birth cohort (n = 619), reporting that children with AD were significantly more likely than healthy control subjects to be sensitized to at least 1 of 6 foods (milk, egg, sesame, peanut, wheat, or cod), with an adjusted odds ratio (aOR) of 8.53 (95% CI, 3.51-20.65; $P < .001$). This association was independent of filaggrin (FLG) loss-of-function mutation inheritance. Equally, there was a positive association between AD and sensitization to individual foods, including egg (aOR, 9.48; 95% CI, 3.77-23.83; $P < .001$), milk (aOR, 9.11; 95% CI, 2.27-36.59; $P = .002$), and peanut (aOR, 4.09; 95% CI, 1.00-13.16.76; $P = 0.05$).

Another wider study which shows the relation between AD and FA was the BAMSE cohort (23) including 2256 newborns, reporting that 27% of patients with AD developed positive SPT responses to food (egg, 21%; peanut, 15%; milk, 8%; and cod, 2%) at 2 years of age. However, the researchers did not include a control group of infants without AD. SPT sensitization among 1501 older children aged 12 to 16 years who were involved in the Danish Adolescent Odense Cohort (TOACS) [24] was also investigated. Although a strongly positive association was demonstrated between current AD and peanut sensitization (16.2% of patients with AD vs. 0.5% of control subjects, $P < 0.05$) during adolescence, no significant differences persisted for milk and egg sensitization.

The Isle of Wight allergy birth cohort (n = 1456), by Arshad *et al.*, [25] reported that at 4 years of age, the highest independent risk factor for AD was SPT sensitization to peanut (odds ratio [OR], 4.65; 95% CI, 1.02-21.34).

5. PHENOTYPES IN AD

Four different clinical phenotypes of AD in early childhood have been identified [26]. Data were obtained from 572 children under 3 years of age with AD. Children in group A (n=141) had early-onset AD with high blood eosinophil counts, serum total immunoglobulin E and rates of sensitization to food allergens. Children in group B (n = 218) had early-onset AD with low blood eosinophil counts, serum total immunoglobulin E and rates of sensitization to both food and inhalant allergens. Children in group C (n=53) had early-onset atopic dermatitis with high C-reactive protein levels and white blood cell counts. Children in group D (n=160) had middle-onset atopic dermatitis with high serum total immunoglobulin E and rates of sensitization to inhalant allergens. Group A had the highest score for AD and TEWL values.

6. PHENOTYPES IN CHILDREN WITH FA AND DA

In FA 3 different phenotypes can be developed:

- 1) As an immediate, non-eczematous IgE reaction. The adverse event starts during the first two hours after the food ingestion with symptoms such as urticaria, angioedema, respiratory and/or gastrointestinal symptoms or anaphylaxis.
- 2) As an eczematous delayed symptom, appearing some hours after the contact with the allergen to 48 hours later.
- 3) As a combination of non-eczematous immediate reaction with delayed eczema (mixed reaction).

In a study including 106 double-blind placebo control food challenges (DBPCFC) in 64 children with AD, 45% developed mixed reactions and 12% only delayed events [27]. Nevertheless, in the Danish cohort DARC [28], during DBPCFC, 95% developed an immediate reaction.

7. AD AND FA EVALUATION

Most of the children suffer from mild eczema (>80%). In the absence of a history of immediate reactions, food allergy investigation is not mandatory. FA can be suspected and ruled out only if AD is moderate to severe regardless of adequate treatment.

The European Academy of Allergy and Clinical Immunology (EAACI) position paper [30] on late eczematous reactions to food in AD recommends further investigations in the following circumstances:

- 1) AD and a history of an immediate reaction against one or more foods;
- 2) Persistent, moderate-to-severe AD, without a history of immediate-reactions to food;
- 3) When a food item is suspected by patients or parents as a trigger factor for persistent AD (without obvious immediate reactions).

Children with AD and FA can have other symptoms such as vomiting, diarrhea and failure to thrive. Nevertheless, it can be more difficult to find the causative allergen in cases of delayed eczematous reactions triggered by food. A detailed clinical history is mandatory, but may not identify the culprit food, as the sensitivity in AD and of other non-IgE mediated reactions can be as low as 25%. Reactions can be delayed by hours to days, making an association with the allergen less straight-forward. If the food is ingested regularly, symptoms may become chronic and are less easily linked to the food causing allergy.

In the young infants, there may be an identifiable link between cow's milk formula feeding or weaning to solid foods, and the onset of symptoms. There may be an association with the mother's diet whilst breastfeeding, as a small amount of an allergen may be added to the infant's diet via the breast milk. Patients and parents should be asked about the time of onset, pattern and severity of eczema; response to previous treatments; possible trigger factors including dietary history, reactions, growth and development.

Allergens demonstrated in vivo (SPT) or in vitro (sIgE) are markers of sensitization which may not cause allergy as sensitized patients may produce IgE to a given protein, without developing symptoms upon exposure to that possible allergen. In a child who has been sensitized to a food (through breast milk) but has never ingested it, investigation should be performed under medical supervision as a reaction can occur [31].

SPT has a high negative predictive value of 95%, but a low positive predictive value of 50% as well as sIgE. The predictive value of food sIgE was investigated in a study [32] including more than 1000 children 3-18 months old with mild, moderate and severe AD without a history of FA who were treated with pimecrolimus. Authors reported low efficiency of sIgE in predicting the development of FA.

The Atopy Patch Test (APT) measures type IV hypersensitivity. It involves the application of food extract directly to the patient's skin with erythema and infiltration assessment after 48-72 hours. APT has high sensitivity but low specificity. A study suggests that there is insufficient evidence for the routine use of atopy patch test for the evaluation of egg and cow's milk allergy [33].

A study [34] compared the sensitivity and specificity of APT versus SPT and measurement of sIgE antibodies to selected foods (cow's milk, hen's egg, wheat, and soy) in 873 children with moderate-to-severe AD without a history of immediate reactions in relation to a positive OFC. APT showed greater sensitivity than SPTs and sIgE in cases of delayed eczematous reactions and improved both sensitivity and specificity as well as the predictive value when combined with SPT and specific IgE. According to a recent EAACI position paper [35], APT cannot yet be recommended in routine clinical practice due to lack of standardization.

In the DARC cohort [28], 52% of the children were sensitized to allergens wheat, being the most frequent allergy-causing food. After OFC only 15% confirmed food allergy, 95% being immediate reactions. The most common food causing allergy was egg.

Usually, the most common food allergens are cow's milk, hen's egg, peanut, and soy in infants and wheat, fish, tree nuts, and shellfish in older children.

Much efficacy has been observed after implementing an elimination diet during 4-6 weeks followed by an OFC [36], always under medical supervision, which can confirm FA with the appearance of eczematous lesions. Anaphylaxis has been described after an elimination diet. In case reactions aroused, FA suspicion is confirmed and the diet without the trigger food should be followed during 6 months with frequent evaluation. Nevertheless, if after the elimination diet eczema persists, FA linked to that specific food can be ruled out. OFC [34] should only be performed when symptoms are mild and the patient is not taking antihistamines. The child should receive a normal serving amount and doses should be given every 20 minutes. SCORAD (SCORing Atopic Dermatitis) should be done before the OFC, two hours and the day after and it will be considered positive when it increases to at least 10 points. If it is negative, the food should be

taken every day with a new SCORAD evaluation in one week.

According to EAACI Guidelines [35-38], if the eczematous reaction is delayed or subjective, a DBPCFC should be performed. If the eczematous reaction is immediate or objective, OFC can be un-blinded.

8. ELIMINATION DIETS

FA parents' perception regarding children with AD is 55%, that is significantly higher than that of parents of children without AD (12%) [38]. Exposure to environmental food allergens induces sensitization which can lead to FA through an impaired skin barrier. However, immune tolerance can be achieved through early oral exposure to food allergens.

Prospective studies from the 1980s led to the hypothesis that total solid food elimination for the first 6 months of life may be beneficial in preventing AD. However, current evidence shows that AD arises before the development of food sensitization and food allergy is associated with severe and chronic AD.

Exclusion diet is generally not recommended unless there is a clinical history of IgE-mediated allergic reactions among young patients with severe disease [39].

In a Cochrane systematic review [40] of 9 randomized trials evaluating dietary exclusions in 421 patients with medically-diagnosed atopic eczema, no evidence of benefit in unselected patients with: egg and milk-free diet (6 trials with 288 patients), elemental diet (2 trials with 48 patients) and few-foods diet (1 trial with 85 patients) was found. Egg-free diet may be beneficial to infants with suspected egg allergy who have positive specific IgE to egg [40].

Empiric diets with the exclusion of milk, egg, nuts, banana, strawberry, chocolate, additives etc would not only be beneficial for eczema but they will also lead to deficiencies in nutrition.

Partially hydrolyzed cow's milk formula might reduce the severity of atopic dermatitis in infants based on a randomized trial [38] with 113 infants younger than 6 months old with AD. They were randomized to partially hydrolyzed or cow's milk formula. Partially hydrolyzed cow's milk formula group had significantly reduced AD severity scores compared to conventional cow's milk formula group at 12 weeks ($p < 0.05$).

Dietary supplements with limited evidence of benefit for atopic eczema include fish oil, and vitamin D plus vitamin E, based on a Cochrane review [40].

Evidence suggests that tolerance pathways may require continued consumption of the food allergen. Avoidance for a period of time may result in the loss of tolerance and increased risk of developing immediate-type allergy and even anaphylaxis to the avoided food. The rate of immediate reactions after an elimination diet is higher than 50%, anaphylaxis occurring in one-third of the patients. They can appear after only a period of 7-14 days.

9. PREVENTION

9.1. Daily Emollient Treatment

As usually AD develops during the first 2 years of life, primary prevention efforts have focused on the prenatal period and early infancy. Daily emollient therapy may prevent atopic dermatitis in high-risk newborns [41], based on 2 randomized trials [42, 43] with 124 healthy term newborns.

There is some more research ongoing [44] relating the intensive and early treatment of the skin to reduce allergic disorders. In the BEEP (Barrier Enhancement for Eczema Prevention) study [45], 124 high-risk newborns have been randomized to receive or not emollients before 3 weeks of life and up to six months. The results show a significant reduction in the cumulative eczema incidence of 22% in the active group compared with the controls (43%). They conclude that the daily use of emollients in high-risk newborns prevents AD development.

Currently, the PreventADALL randomized study [46] is also ongoing, examining the efficacy of primary prevention of allergic diseases such as AD and FA by regular intake of six-food-items from 3 months of age and emollient application in the general population in Norway and Sweden.

Optimization of skincare is cheap and plays a key role in the management of a child with AD and FA. AD has a remitting-relapsing course and can improve and worsen without an obvious trigger. AD is commonly undertreated and many parents report significant improvement or even resolution of eczematous lesions with appropriate topical management.

9.2. Breastfeeding and Hydrolyzed Formulas

Relating food elimination diets of the mother during pregnancy and breastfeeding studies do not give positive results about AD and FA prevention in the newborns and infants [47, 48]. Breastfeeding is recommended with the introduction of solid foods from 4 months of age. If this is not possible, hydrolyzed formulas are recommended in high-risk patients [49]. Prolonged breastfeeding (>12 months) might increase the risk of AD in children aged < 5 years regardless of parental history of DA [50]. Up to now, the evidence is still not sufficiently robust to make firm conclusions and not strong enough to recommend changing the diet or supplements of pregnant or breastfeeding women at normal or high risk [51].

Many studies have been focused on high-risk children. The German Infant Nutritional Intervention (GINI) program [52] recruited 2252 infants with a heredity risk for atopy and conducted a prospective, double-blind randomized controlled trial to study the effectiveness of hydrolyzed formulas for allergy prevention. This study showed an evidence that hydrolyzed formula plays a role in the prevention of atopic dermatitis (AD), but not of allergic respiratory diseases. Some national and international pediatric societies have implemented the use of hydrolyzed formulas to prevent FA in their recommendations for children at risk who cannot exclusively breastfeed in the first 4–6 months of life. For the same infants, a previous Cochrane systematic review [53], in 2006, have already concluded that there was limited evidence that prolonged feeding with a hydrolyzed formula

compared to a cow's milk formula reduces infant and childhood allergy and infant CMA. Recently, the EAACI Food Allergy and Anaphylaxis Guidelines Group reviewed literature concluding that the use of extensively hydrolyzed whey or casein formula in infants at high risk for the first 4 months may have benefits in preventing food allergy. More definitive and randomized controlled trials are needed.

9.3. Introduction of Solid Foods

The LEAP (Learning Early about Peanut Allergy) [54] study has led to a change in the perception of FA. It is a randomized study, including 640 infants 4–11 months old with severe eczema, egg allergy or both. They were randomized to consume or not peanut up to 60 months old. The results show that in children at high risk, the prevalence of peanut allergy was higher in the group who followed a peanut-free diet. The severity of SCORAD did not change between the two groups. Given the success of early peanut introduction in peanut allergy prevention in high-risk infants (infants with severe eczema and/or egg allergy), these authors next evaluated exclusively standard-risk breastfed infants at 3 months of age, assigning them randomly to early introduction of six allergenic foods (peanut, cooked egg, cow's milk, sesame, whitefish, and wheat) or to usual food introduction at 6 months of age (EAT study) [55]. Although the intent to treat protocol analysis did not show significant differences in food allergies between the groups, the per-protocol analysis demonstrated a lower food allergy prevalence in the early introduction group (2.4 vs. 7.3%, $P = 0.01$).

The HYGIENE study by Turati [56] included 451 children vs 451 controls with or without familiar atopic history. They concluded that the introduction of solid foods at 4–5 months of age was inversely related to AD risk compared with those who were only breastfed. The introduction of more solid foods at 4–5 months reduces the risk of AD development.

The Prevention of Egg allergy with Tiny amount InTake (PETIT) study [57] investigated the effects of early introduction of heated egg powder to high-risk Japanese infants with AD on the development of egg allergy. The intervention group which received 50 mg of heated whole egg powder between 6–9 months of age, followed by 250 mg between 9–12 months of age, had a 30% lower risk of developing challenge-proven hen's egg allergy at 12 months of age, compared to the placebo group.

9.4. Pre- Probiotics And Vitamins

There are many studies [58] ongoing on the use of pre and probiotics without clear results.

A partially hydrolyzed formula supplemented with probiotic does not prevent the development of AD during the first year of life in infants at high risk [59]. The EAACI Food Allergy and Anaphylaxis Guidelines [60] do not show either enough evidence to recommend probiotics to prevent food allergy.

In patients with AD, the supplementation with vitamin D, especially if they have low levels, can be recommended [58].

10. TREATMENT

In general, the management of AD in children involves a stepwise approach. Topical treatment includes the regular application of emollients to aid in epidermal barrier repair. Anti-inflammatory therapy is also advised with topical corticosteroids, which can be mild, moderate, potent or very potent; and calcineurin inhibitors, which are licensed to be used in children over the age of two. These treatments can be applied in a reactive way when the illness is active, while a proactive approach would be to use them even when the skin is not damaged in order to treat the subclinical inflammation. In one study [61], a significant decrease in IgE and sIgE to egg components was shown in the proactive treatment group study. In another study [62] in which proactive treatment was used before 4 months of age, children had lower egg allergy prevalence rates at age 18 months compared with the ones in whom the treatment was initiated later than 5 months of age (9.1% vs. 24.2%). So, a proactive approach in AD can decrease the risk of FA.

Crisaborole, a topical PDE-4 inhibitor, was FDA approved in late 2016 for the treatment of mild-to-moderate AD in adults and children older than 2 years.

The PACI Study [44] (Early aggressive intervention for infantile atopic dermatitis to prevent development of food allergy) which is ongoing, has included 650 patients who had developed an itchy rash during the first 28 days of life. The patients were randomized at 7-13 weeks of life in two groups: one receiving proactive treatment with local corticosteroids vs conventional 1:1. An OFC will be performed at 28 weeks of life.

The recent and emerging availability of TH2-targeting therapy provides another opportunity for preventing the development of atopic comorbidities because these targets are downstream of several components involved in the atopic march (e.g., IL-33, TSLP, and IL-4/IL-13). The possibility of an early intervention that targets TH2 immunity is supported by studies showing strong TH2 skewing in both non-injured and injured AD skin [63].

CONCLUSION

AD and FA are common conditions appearing in childhood that are closely linked. 30% of children with moderate to severe eczema suffer from FA. There is evidence that non-justified elimination diets should not be advised in the treatment of children with AD. Sensitization to a food (positive SPT and/or sIgE) does not mean allergy and the unjustified elimination of that specific food can be harmful and lead to loss of tolerance with anaphylaxis when reintroduced.

There is strong evidence for the link between early-onset AD and the development of other allergic diseases in later life. Several preventive interventions such as early regular emollient use and early introduction of peanut and egg in high-risk infants have shown promising results for the prevention of AD as well as peanut and egg allergy.

LIST OF ABBREVIATIONS

AD = Atopic Dermatitis
APT = Atopy Patch Test

DBPCFC = Double-blind, Placebo-controlled Food Challenge
FA = Food Allergy
FC = Food Challenge Test
OVA = Ovalbumin
SCORAD = SCORing Atopic Dermatitis
s-IgE = Specific IgE
SPT = Skin Prick Test

CONSENT FOR PUBLICATION

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CONFLICT OF INTEREST

The authors declare no conflict of interest, financial or otherwise.

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