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Original article

EPICUTANEOUS PATCH TEST RESULTS IN CHILDREN WITH ATOPIC DERMATITIS

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Abstract

Atopic dermatitis (AD) is one of the most common inflammatory diseases, occurring in 20% of children and 10% of adults in highly developed countries. It is a multifactorial disease with a complex pathogenesis, where a significant role is played by the disruption of the epidermal barrier and immune dysregulation. The wide spectrum of possible clinical manifestations complicates the categorization of these patients. Allergic contact dermatitis (ACD) is not rare in patients with AD. The aim of this study was to evaluate the results of epicutaneous patch testing with a standard series of contact allergens in children with AD and suspected for ACD and to compare the results with disease activity. The study was conducted at the University Clinic for Dermatology, Skopje, in patients with AD, aged ≤18 years. The study included 12 children, 5 girls and 7 boys, aged between 2-13 years. The patch test was negative only in one patient, two patients had only 2 positive results, and 9 patients had 4 or more than 4 positive results. In our series, ACD in children with AD was very common (11 out of 12 patients). The most common allergens were cobalt chloride, potassium dichromate, and propolis 10%.

Keywords: atopic dermatitis, contact dermatitis, PATCH test, children

Introduction

Atopic dermatitis (AD), or atopic eczema, is a long-term, recurring inflammatory skin condition marked by repeated outbreaks of eczematous rashes accompanied by severe itching. It ranks among the most prevalent skin inflammatory diseases, affecting as many as 20% of children and 10% of adults in developed nations [1,2].

This condition impacts individuals of all ages and ethnic backgrounds and has significant emotional and social consequences for both patients and their families. AD is the leading contributor to the global burden of skin diseases. While it can develop at any age, it most commonly begins in infancy - typically between 3 to 6 months of age in 45% of cases - and in 70% of cases, symptoms appear by age 5[2].

AD is a multifaceted disease influenced by numerous internal and external factors. Individuals with AD are more likely to develop other allergic conditions such as food allergies, allergic rhinitis or asthma later in life. The disease progresses through two main phases. In the initial sensitization phase, environmental allergens are processed in lymph nodes, leading to the creation of allergen-specific T cells. Upon re-exposure (elicitation phase), these T cells move to the skin and trigger inflammation, causing symptoms like redness, swelling, itching, and blistering characteristic of acute AD[3].

Genetics also play a key role in AD. Mutations that reduce the function of the *filaggrin* (FLG) gene - a gene crucial for skin barrier integrity - are among the most consistently observed genetic risk factors [2,3]. Despite the genetic predisposition, rising global rates of AD underscore the importance of environmental influences[2].

Currently, clinical evaluation by a healthcare professional is the gold standard for diagnosing AD, as there are no definitive symptoms or lab tests for the condition. Itching is the hallmark symptom, and eczema usually appears in predictable areas such as the face, neck, and skin folds, though the affected sites vary with age. Hanifin et al. established a diagnostic approach based on four major and several minor criteria[4].

Allergic contact dermatitis (ACD) is delayed type IV hypersensitivity skin reaction to environmental allergens[5]. In children, patch testing for ACD is performed in fewer than 10% of cases [6], largely due to practical challenges such as limited skin area and ensuring patient compliance throughout patch testing. As a result, many children with AD are not tested for ACD, leading to underdiagnosis of the condition[6-8]. As both ACD and AD have similar clinical presentations and are characterized by spongiotic dermatitis on skin biopsy, many children with AD are not referred for patch testing and allergic contact dermatitis is frequently overlooked[9].

Aim

This study aimed to assess the outcomes of patch testing (PT) using the European Baseline Series and Cosmetic Series of contact allergens in pediatric patients diagnosed with atopic dermatitis (AD) and/or suspected for allergic contact dermatitis (ACD).

Material and methods

We carried out a cross-sectional study of 12 symptomatic children with AD, who had patch testing performed at the PHI University Clinic for Dermatology, Skopje.

The patients aged ≤18 years with AD according to the Hanifin and Rajka criteria for at least 6 months prior to the study, discontinuation of antihistamine systemic therapy for at least 2 weeks prior to the study, and topical corticosteroid therapy for at least 7 days prior to the study. Deteriorating AD and localized dermatitis were indications for performing PT. The topographic phenotype was specified according to the areas affected and divided into palmo-plantar, periocular, face, scalp, flexural and inverse types. Prior to testing, skin phototype of each patient was determined according to the Fitzpatrick classification.

The European Baseline Series (EBS) and Cosmetic series were used for PT. PT was performed by applying purified allergen preparations in vaseline to chambers with a diameter of 12 mm, placed on a Scanpor strip to non-irritated, non-abrasive and non-adherent skin of the upper back. PT was read at 48 and 72 hours after application, according to testing criteria and standard manufacturer protocols (Chemotechnique MB Diagnostics AB, Sweden), assessing for appearance of erythema, and number and distribution pattern of papules. A selected palette of the most common allergens relevant to children with AD was applied to the interscapular space.

Results

Table 1: Results from PATCH testing

Sex	Age (years)	Phototype	Topographic phenotype	Positive PATCH test
F	10	2	palmoplantar	-Potassium dichromate - Peru balsam 25%
M	10	3	inverse	-Triclosan 2.0%
M	13	3	periocular perioral	-Benzyl salicylate 10% -Phenyl mercuric cetate 0.01% -Stearyl alcohol 30% - Caine mix 10% - Cobalt chloride -Thimerosal 0.1%
F	13	3	periocular perioral flexures	-Benzyl salicylate 10% - Cobalt chloride - Cetyl alcohol 5% - Potassium dichromate
M	9	2	palmoplantar	- Propolis 10% - Hydroabietyl alcohol 10% - Nickel sulfate 5% - Fragnance mix 8.0%
F	6	2	palmoplantar	- Methylisthiazolinone - Methylchloroisothiazolinone - Methyldibromo glutanoronitrile 0.5% -Potassium dichromate
M	11	3	inverse	negative
M	5	3	inverse	-Sesquiterpene lactone mix 0.1%
M	3	4	inverse	- Methylisthiazolinone - Methylchloroisothiazolinone - Methyldibromo glutanoronitrile 0.5% - Propolis 10% - Potassium dichromate
F	7	3	inverse	- Caine mix 10% 2 -Hydroxyethyl methacrylate 2% -Colophonium 20% -Epoxy resin, Bisphenol A 1% - Nickel sulfate 5% -Cobalt chloride
F	8	2	palmoplantar	- Hydroxyisohexyl 3 cyclohexane carboxaldehyde - Propolis 10% - Tixocortol 21 pivalate - Cobalt chloride - Neomycin sulfate 20% - Fragnance mix 8.0% - Methylisthiazolinone - Potassium dichromate
M	2	2	inverse	- Cobalt chloride - Propolis 10%

This study aimed to assess the patch test results and the prevalence of allergens in children with atopic dermatitis (AD), focusing on the topographic distribution of dermatitis and the corresponding allergenic sensitivities.

The study included 12 children (5 girls, 7 boys) aged between 2 and 13 years (mean age 8.08 years) with diagnosed AD. According to the Fitzpatrick phototype classification, 5 children (41.7%) were phototype II, 6 children (50%) were phototype III, and 1 child (8.3%) was phototype IV. The topographic distribution of dermatitis showed a generalized presentation, with 6 children (50%) exhibiting an inverse (flexural) distribution, 4 children (33.3%) presenting with palmo-plantar involvement, and 2 children (16.7%) having only facial involvement.

Patch testing revealed that only 1 child (8.3%) had a negative patch test, 2 children (16.7%) had two positive results, and 9 children (75%) had four or more positive results. The most frequent metal allergens were Cobalt chloride and Potassium dichromate, identified in 5 children (41.7%) each. The most common non-metal allergen was Propolis, found in 4 children (33.3%), and Methylisothiazolinone was positive in 3 children (25%). Other significant allergens included Caine mix 10%, Benzyl salicylate 10%, Nickel sulfate 5%, Fragrance mix 8.0%, Methyldibromo glutaronitrile 0.5%, and Methylchloroisothiazolinone, each found in 2 children (16.7%). Additionally, single positive results (8.3%) were observed for Peru balsam 25%, Triclosan 2.0% Thimerosal 0.1%, Phenyl mercuric acetate 0.01%, Stearyl alcohol 30%, Cetyl alcohol 5%, Hydroabietyl alcohol 10%, Hydroxyethyl methacrylate 2%, Sesquiterpene lactone mix 0.1%, Colophonium 20%, Epoxy resin (Bisphenol A) 1%, Neomycin sulfate 20%, Tixocortol-21-pivalate, and Hydroxyisohexyl 3-cyclohexene carboxaldehyde.

This study demonstrated a diverse spectrum of allergic sensitivities in children with atopic dermatitis, with significant reactions to both metal and non-metal allergens. A high prevalence of positive patch test results, particularly involving Cobalt chloride, Potassium dichromate, and Propolis, was observed, highlighting the importance of comprehensive allergen testing in the management of AD in pediatric populations.

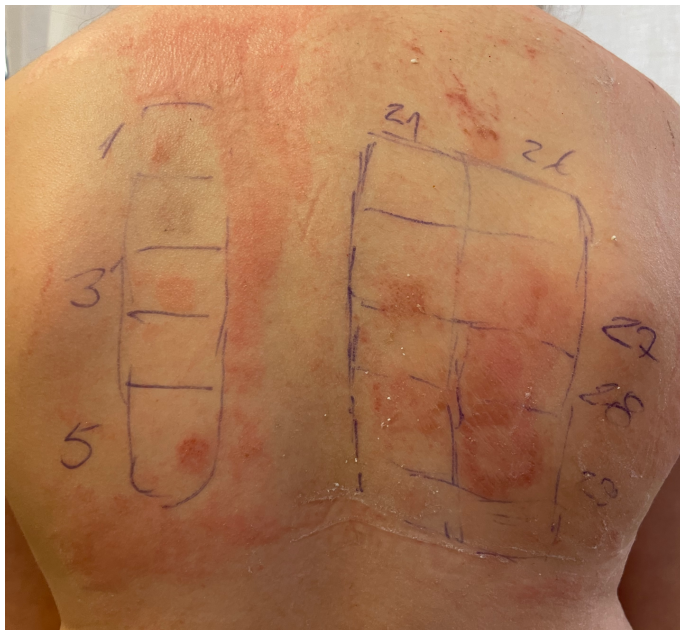

Fig. 1. An 8-year-old patient representing strong positive PATCH test results on: Fragnance mix 8.0%, Hydroxyisohexyl 3 cyclohexane carboxaldehyde, Methylisthiazolinone, Neomycin sulfate 20%, Cobalt chloride, Tixocortol 21 pivalate, Propolis 10%. Plaster dermatitis was observed, and the patient was not tested for adhesives.

Discussion

ACD was once considered a rare condition in the pediatric population. However, recent studies have indicated that its prevalence is relatively common and appears to be increasing among children. Current trends, including the use of toys, hobbies, and personal care products, may contribute to the introduction of new allergens or the resurgence of previously identified allergens, thereby rendering ACD a dynamic and evolving concern in pediatric dermatology. Historically, patch testing has been employed to investigate the association between atopic dermatitis (AD) and contact allergies. Aeroallergens and contact allergens are both relevant in AD patients, as they contribute to the development of sensitization and exacerbate cutaneous symptoms.

The European Task Force on Atopic Dermatitis (ETFAD) has developed a standardized APT technique[10]. In contrast with skin prick tests, the APT might even detect a relevant sensitization in the absence of specific IgE[11]. Clinically, Fortina et al.[12] identified that 61% of children under the age of 3 with AD exhibited a reaction to at least one sensitizer present in standard patch test baselines. Likewise, Czarnobilska et al.[12] observed that 48.5% of 7–8-year-olds with a history of atopy showed positive reactions to at least one substance in regular patch test baselines. Lastly, Mortz et al.[13] documented the coexistence of contact dermatitis in 21.3% of adolescents aged 12–16 diagnosed with atopic.

In contemporary clinical practice, ACD is increasingly recognized in the pediatric population, with the prevalence of positive patch test reactions ranging from 14% to 70% among children undergoing patch testing[7-14].

Among the allergens most commonly identified in these cases, cobalt chloride and potassium dichromate are frequently implicated. Cobalt chloride is a well-known metal allergen responsible for delayed hypersensitivity reactions. It affects 1–4% of the general population and can develop at any age, including in childhood[15]. Cobalt is commonly used as a binding agent in the manufacturing of "hard" metals and is also found in a variety of consumer products, including jewelry, cosmetics, leather goods, clothing, shoes, and dental alloys. Potassium dichromate, another significant allergen, is present in chrome-tanned leather goods, certain cosmetics, disinfectants, bleach agents, unlit match heads, and radiator coolants[16]. Both cobalt chloride and potassium dichromate are commonly associated with allergic reactions in children with AD, as demonstrated in a systematic review of patch test results in this population[17]. Previous studies have reported the same pattern of sensitization in patients with AD[17-19].

Malajian and Belsito in their study[20] observed that positive patch test reactions to nickel sulfate, cobalt chloride, and potassium dichromate were significantly more frequent among patients with AD compared to control groups. In the present study, propolis 10% emerged as the most frequently positive non-metal allergen, ranking as the second most common allergen overall. Propolis is commonly found in products such as mouth lozenges, cough syrups, ointments, lotions, and oral medications. Methylisothiazolinone (MI), introduced as a standalone preservative in the early 2000s, became widely used in cosmetics beginning in 2005. Prior to this, MI was used exclusively in combination with methylchloroisothiazolinone (MCI). Both MI and MCI are now recognized as prevalent causes of preservative-related contact allergies[21]. MI is used in paints, adhesives, cleaners, and household products, including wet wipes, shampoos, and liquid laundry detergents. Caine mix 10% (benzocaine), typically found in pharmaceutical formulations for cough suppression and toothache relief, is also a recognized allergen. Benzyl salicylate 10%, commonly present in cosmetics such as sunscreen, perfumes, shampoos, and lotions, is another allergenic substance identified in the current study.

Nickel, a naturally occurring silver-colored metal, is commonly found in jewelry, coins, eyeglass frames, and various other items. It is also present in trace amounts in numerous food

products[22]. In 2007, the American Contact Dermatitis Society (ACDS) designated fragrance mix as the "Contact Allergen of the Year"[23]. Fragrance mix comprises eight individual fragrances frequently used in patch testing to identify fragrance allergies. These fragrances are prevalent in a wide range of consumer products, including cosmetics, deodorants, detergents, personal hygiene items, and flavoring agents. In this review, fragrance emerged as a frequent sensitizer among children with AD undergoing patch testing, particularly in cases where AD was exacerbated or when ACD was suspected[16]. However, fragrance allergy does not appear to be as prevalent among children with AD without concurrent skin symptoms. Methyldibromo glutaronitrile 0.5% and methylchloroisothiazolinone are common allergens found in products such as baby wipes, shampoos, bubble baths, detergents, and sunscreens.

Both genetic predispositions and environmental exposures - such as air pollution, suboptimal housing conditions, and various lifestyle factors - have been implicated in the development and exacerbation of allergic diseases. Emerging evidence from epidemiological, immunological, and clinical studies suggests a notable overlap between allergic contact dermatitis (ACD) and atopic dermatitis (AD), with individuals diagnosed with AD exhibiting an increased susceptibility to ACD. This heightened risk is attributed to impaired skin barrier function and the frequent application of topical products containing potential allergens[25]. Patch testing is recommended in pediatric populations when ACD is suspected, in patients with concurrent dermatoses potentially worsened by contact allergens (e.g., atopic or seborrheic dermatitis), and in cases of persistent eczema with an undetermined cause. Despite its prevalence, affecting an estimated 20% of individuals under 18 years of age, ACD remains under-researched in pediatric cohorts [15-26].

Conclusion

Children with atopic dermatitis (AD) are significantly more likely to exhibit positive patch test (PT) reactions, indicating a higher prevalence of allergic contact dermatitis (ACD) in this population. Patch testing should be considered, particularly in cases of exacerbated AD, as clinically relevant contact allergies are common. The most frequently identified allergens in children include cobalt chloride, potassium dichromate, and propolis 10%. This information is crucial for developing preventive strategies and tailoring management plans. Implementing educational programs targeted at healthcare providers, children with AD, and their families can aid in recognizing and avoiding common allergens, particularly metals and fragrances, thus potentially reducing disease severity and improving quality of life in pediatric patients with AD.

Conflict of interest statement. None declared.

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