ORIGINAL ARTICLE

Association between atopic dermatitis and contact sensitization: A systematic review and meta-analysis

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Background: It is unclear whether patients with atopic dermatitis (AD) have an altered prevalence or risk for contact sensitization. Increased exposure to chemicals in topical products together with impaired skin barrier function suggest a higher risk, whereas the immune profile suggests a lower risk.

Objective: To perform a systematic review and meta-analysis of the association between AD and contact sensitization.

Methods: The PubMed/Medline, Embase, and Cochrane databases were searched for articles that reported on contact sensitization in individuals with and without AD.

Results: The literature search yielded 10,083 citations; 417 were selected based on title and abstract screening and 74 met inclusion criteria. In a pooled analysis, no significant difference in contact sensitization between AD and controls was evident (random effects model odds ratio [OR] = 0.891; 95% confidence interval [CI] = 0.771-1.03). There was a positive correlation in studies that compared AD patients with individuals from the general population (OR 1.50, 95% CI 1.23-1.93) but an inverse association when comparing with referred populations (OR 0.753, 95% CI 0.63-0.90).

Limitations: Included studies used different tools to diagnose AD and did not always provide information on current or past disease. Patch test allergens varied between studies.

Conclusion: No overall relationship between AD and contact sensitization was found. We recommend that clinicians consider patch testing AD patients when allergic contact dermatitis is suspected. (J Am Acad Dermatol http://dx.doi.org/10.1016/j.jaad.2017.02.001.)

Key words: allergic contact dermatitis; atopic dermatitis; atopic risk factors; atopy; chromium; contact allergy; contact sensitization; eczema.

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Conflicts of interest: Drs C. R. Hamann and D. Hamann are first degree relatives of Curtis Hamann, owner of SmartPractice, a producer of contact allergy diagnostic testing materials. Dr Egeberg has received research funding from Pfizer and Eli Lilly, and honoraria for consulting and speaking for Pfizer, Eli Lilly, Novartis, Galderma, and Janssen Pharmaceuticals. Drs Johansen and Silverberg have no conflicts of interest. Dr Thyssen is supported by an unrestricted grant from the Lundbeck Foundation and has attended advisory board meetings for Roche and Sanofi-Genzyme.

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Atopic dermatitis (AD) is a chronic relapsing, pruritic inflammatory skin condition that most often begins in early childhood.[1] The risk for AD is increased in individuals with primary skin-barrier impairment, eg, mutations in the common *filaggrin* gene, but also in individuals with primary immune dysregulation.[2,3]

Allergic contact dermatitis (ACD) is a type IV hypersensitivity reaction caused by re-exposure to a cutaneous contact allergen in a presensitized individual. ACD is diagnosed via patch testing, the process of applying contact allergens to the skin under occlusion and visually grading the skin inflammatory response. Contact sensitivity is the term used to describe a positive patch test reaction. To diagnose ACD in a patient, he or she must have a contact sensitivity, and a dermatitis with clinically relevant exposure to said contact allergen. It has long been debated whether or not patients with AD have an altered prevalence or increased risk for contact sensitization when compared with controls. Several factors might affect this relationship as recently discussed in detail.[4] In favor of the increased occurrence of contact sensitization among patients with AD includes evidence of a nearly twofold—increased skin absorption of chemicals including irritants and contact allergens in AD skin.[3,5,6] In addition, patients with AD frequently use, as a part of recommended treatment, topical medicaments and moisturizers.[7] Unfortunately, moisturizers might contain contact allergens, as illustrated in a recent study from the United States where a large proportion of 187 so-called hypoallergenic, pediatric cosmetic products contained contact sensitizers, including the potent preservative methylisothiazolinone (seen in 10%).[8]

However, there is also compelling evidence in favor of reduced contact sensitization in AD populations; notably, experimental studies have found an increased elicitation threshold in AD patients compared with controls.[9-12]

Epidemiologic studies investigating contact sensitization prevalence in patients with AD compared with those without have shown mixed results.[10,11,13-16] To increase insight of this relationship, we performed a systematic review and meta-analysis of the literature.

CAPSULE SUMMARY

- It is unclear whether individuals with atopic dermatitis have an altered risk for contact sensitization.
- This meta-analysis showed no significant association between atopic dermatitis and contact sensitization. However, contact sensitization was increased in individuals with atopic dermatitis in general population studies.
- Individuals with atopic dermatitis have similar rates of contact sensitization as individuals without, and clinicians should consider patch testing when allergic contact dermatitis is suspected.

MATERIALS AND METHODS

Literature search

We searched the databases PubMed/Medline (1946-present), EMBASE (1947-present), and Cochrane Library(1992-present) through October 2016 using the search terms ("atopic dermatitis" OR "atopic eczema" OR "atopy") AND ("allergic contact dermatitis" OR "contact allergy" OR "contact sensitization" OR "patch test"). Title and abstract review was performed, and articles were excluded if there was no indication that they reported prevalence of contact sensitization in AD and non-AD populations. Studies published online, in-print, and in-press from all years, written in any language were considered. Studies that used nonscreening patch testing series or only evaluated contact sensitization to specific allergens were included.

Studies that evaluated prevalence of contact sensitization in the general population, contact sensitization in populations of patients referred for patch testing, and preestablished AD patients with matched controls were all included. For this analysis, we focused on studies evaluating individuals specifically with AD. Studies that evaluated patients with undifferentiated atopic syndrome or atopy, ie, a combination of AD, allergic asthma, or allergic rhinoconjunctivitis, were excluded. Articles that evaluated atopy patch test sensitivity or aeroallergen sensitivity were also excluded.

Data extraction and exclusion

Manuscripts were reviewed and the following data points were extracted: total number of individuals patch tested, total number of individuals with and without AD in the patch tested population, total number of AD patients and non-AD patients who had at least 1 positive patch test reaction. In addition, individual allergen patch test data were collected for the allergens nickel, cobalt, chromium, sesquiterpine lactone mix (SL), and Compositae mix, given previous research highlighting their possible relationship to AD.[17,18] Mode of AD diagnosis, patch testing series allergens used, reading days, and location and dates of patch testing were noted for each study. The