Frequency of Contact Allergens in Pediatric Patients with Atopic Dermatitis

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ABSTRACT

Objective: The authors compared the prevalence of positive patch tests in atopic pediatric patients versus nonatopic controls and sought to determine if statistically significant allergen prevalence differences existed between the two groups. **Design:** Retrospective chart review. **Setting:** Rady Children's Hospital, San Diego, California. **Participants:** Patients with suspected allergic contact dermatitis between the ages of 6 and 18 years who had been enrolled in the Pediatric Research Equity Act Thin-layer Rapid Use Epicutaneous Test trial. **Measurements:** Statistical analysis used Z-scores to compare associations between positive reactions in atopic versus nonatopic patients and the prevalence of individual chemicals in either group. **Results:** Results showed that at least one allergen reaction was noted in 78 percent (n=79) of the patients, 89 percent (n=48) in atopic patients, and 66 percent (n= 31) in the nonatopic patients (Z-score 2.78). Eczema area and severity index scores ranged from 0 to 41.75. Eczema area and severity index scores greater than 10 correlated with a higher probability of more than three positive patch tests (Z-score [-]3.28). Statistically significant differences were also observed between atopic and nonatopic patients in regards to contact allergens, with 20 percent (n=11) of atopic patients exhibiting positive patch tests to *Myroxylon pereirae* and 19 percent (n=10) of those with atopic dermatitis having reactions to fragrance mix. **Conclusion:** The authors concur with prior studies that performing systematic patch testing is indicated in children with moderate-to-severe atopic dermatitis, given the high rate of contact allergy in the atopic group, especially those with eczema area and severity index scores greater than 10. Furthermore, prevention through exposure avoidance to the most frequent contact allergens, especially fragrances in patients with atopic dermatitis, is recommended.
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Recent estimates of contact allergy in pediatric patients referred for patch testing range from 41 to 77 percent.[1] In this study, the authors retrospectively analyzed the data from the Pediatric Research Equity Act (PREA) Thin-Layer Rapid Use Epicutaneous (T.R.U.E.) Test study, which reported on the safety and efficacy of panels 1.1, 2.1, and 3.1. The authors' goal was to compare the prevalence of positive patch tests (PPT) in atopic pediatric patients versus nonatopic controls. Their purpose was also to determine if there were statistically significant allergen prevalence differences between the two groups.

METHODS/MATERIALS

Patients included those with suspected allergic contact dermatitis between the ages of 6 and 18 years who had been enrolled in the PREA T.R.U.E. Test trial. A history of atopic dermatitis was recorded during the initial evaluation, and prior to the patch test, the diagnosis had been confirmed using Hanifin and Rajka criteria. Eczema area and severity index (EASI) scores[2] were calculated for atopic patients. The patients had undergone patch testing with the T.R.U.E. Test panels 1.1, 2.1, and 3.1 (SmartPractice, Phoenix, Arizona) per the research design protocol. There were five visits, with Visit 1 (Day 0/D0) being patch application; Visit

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TABLE 1. Ten most common allergens* and their relationship to atopic dermatitis and nonatopic dermatitis

ALLERGEN NAME	AD	NON-AD	TOTAL	Z–SCORE	STATISTICAL SIGNIFICANCE
	% REACTION (N)	% REACTION (N)	% (n)		(Y=YES, N=NO)
1. Nickel sulphate	35% (19)	26% (12)	31% (31)	1.05	N
2. Wool alcohols	24% (13)	11% (5)	18% (18)	1.76	N
3. PTBPFR	15% (8)	15% (7)	15% (15)	-0.01	N
4. Myroxylon pereirae	20% (11)	2% (1)	12% (12)	2.83	Y
5. Cobalt	13% (7)	9% (4)	11% (11)	0.72	N
6. Formaldehyde	15% (8)	4% (2)	10% (10)	1.77	N
7. Fragrance mix 1	19% (10)	0% (0)	10% (10)	3.11	Y
8. Colophonium	13% (7)	4% (2)	9% (9)	1.53	N
9. Potassium Dichromate	11% (6)	4% (2)	8% (8)	1.27	N
9. Neomycin sulphate	7% (4)	9% (4)	8% (8)	-0.2	N
10. Tixocortol-21-pivalate	11% (6)	2% (1)	7% (7)	1.77	N

* Allergens tied for 6th and 9th place. AD=atopic dermatitis

2 (Day 2/D2) patch removal; and Visit 3 (Day 3/D3), Visit 4 (Day 7/D7), and Visit 5 (3 weeks) being follow up. Data from Visits 3 and 4 were combined to record PPT rates in this analysis.

Statistical analysis used Z-scores to compare associations between positive reactions in atopic versus nonatopic patients and the prevalence of individual chemicals in either group. A Z-score ≥1.96 or ≤-1.96 was determined to be of statistical significance. The absolute value of 1.96 would indicate that the two percentages are different at a 95-percent confidence interval.

RESULTS

There were 101 patients who had completed the study—48 males and 53 females, ages 6 to 18 years (mean 11.66 years). Of these, 54 patients had met Hanifin and Rajka criteria for a diagnosis of atopic dermatitis (53%). At least one allergen reaction was noted in 78 percent (n=79) of the patients, 89 percent (n=48) in atopic patients and 66 percent (n= 31) in the nonatopic patients (Z-score 2.78). EASI scores ranged from 0 to 41.75. EASI scores greater than 10 correlated with a higher probability of more than three PPTs (Z-score [-]3.28).

The most common allergens were nickel sulfate (31%), followed by wool alcohols (18%), p-tert-butylphenol formaldehyde resin (PTBPFR) (15%), *Myroxylon pereirae* (12%), cobalt (11%), formaldehyde (10%), fragrance mix 1 [a-amyl cinnamal, cinnamal, eugenol, geraniol, hydroxy-citronellal, isoeugenol, Evernia prunastri] (10%), colophonium (9%), potassium dichromate (8%), neomycin sulfate (8%), and tixocortol-21-pivalate (7%). Statistically significant differences between atopic dermatitis and nonatopic patients were observed, with 20 percent (n=11) of atopic patients exhibiting positive responses to *Myroxylon pereirae* and 19 percent (n=10) of those with atopic dermatitis having reactions to fragrance mix 1 (Table 1).

DISCUSSION

The frequency of contact allergies in the course of atopic dermatitis, especially in children, is largely underestimated.[3] In a recent study on contact sensitization rates in patients with atopic dermatitis, Belhadjali et al[4] reported PPT results in 50 percent of adults and 39.7 percent of children.[4] Importantly, this study found a correlation between the prevalence of contact sensitization and both the severity of atopic dermatitis and the duration of the atopic dermatitis course.[4] Likewise, in the study reported in this article, a higher EASI score correlated with a higher probability of more than three PPTs. In addition, the authors found at least one PPT in 88 percent of the atopic patients, a significantly higher rate than what Belhadjali had reported. This result was statistically significant when compared to the percentage of PPT results in the nonatopic dermatitis population and reflects the significant number of patients with moderate-to-severe atopic dermatitis who were enrolled in the study.

In 1999, Giordano et al[3] evaluated 137 children with atopic dermatitis and found contact sensitization in 43 percent of all children tested, with the most frequent contact allergens being: metals (19.3%), fragrance (4.4%), *Myroxylon pereirae* (2.6%), wool alcohols (4.4%), neomycin sulfate (2.6%), and emollients (2.6%). A decade later, these same allergens are prevalent, as evidenced by the study reported in this article. Furthermore, when compared to nonatopic dermatitis patients, atopic dermatitis patients were significantly more likely to be allergic to fragrances, including *Myroxylon pereirae*. Notable differences the authors saw in their patient population compared with the Giordano study were the presence of contact sensitization to corticosteroids as well as a higher percentage of PTBPFR and formaldehyde contact allergy. The PTBPFR correlated with the number of patients referred for sports gear-associated dermatitis and the formaldehyde with personal hygiene products, as previously reported.[5,6]

Given the prevalence of PPTs to allergens that are also known irritants, such as fragrance, it is of particular importance to note that none of the reactions appeared until at least the third visit and that patients also reacted to their personal care products containing these same allergens on use testing. Moreover, patients improved upon source avoidance. This also indicates the clinical relevance of the patients' PPTs, a pivotal point in patch testing.

One limitation of this study was that patients were patch tested only to allergens included in the T.R.U.E. Test. There are several additional contact allergens that have frequently been reported for which prevalence and relevance in our patient population are of interest, especially among atopic pediatric patients."

In conclusion, the authors concur with prior studies that performing systematic patch testing is a necessity in children with moderate-to-severe atopic dermatitis whose condition is refractory to treatment or whose history is suggestive of allergic contact dermatitis. Furthermore, given the high prevalence of the same allergens a decade later, the authors agree that prevention through exposure avoidance from an early age to the most frequent contact allergens, especially fragrances in patients with atopic dermatitis, is the most prudent measure.

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