

ORIGINAL ARTICLE

Cutaneous delayed-type hypersensitivity in patients with atopic dermatitis: Reactivity to surfactants

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Background: Patients with atopic dermatitis (AD) have abnormalities in skin barrier function, and are predisposed to developing cutaneous delayed-type hypersensitivity. Soap and detergents are known to exacerbate the breakdown of the skin barrier.

Objective: We sought to assess whether atopic patients in our database were more likely than nonatopic patients to patch test positive to the surfactants cocamidopropyl betaine (CAPB) and cocamide diethanolamide (DEA), or to the surfactant precursor amidoamine.

Methods: Between January 1, 2001, and the present, a total of 1674 patients underwent patch testing to the North American Contact Dermatitis Group standard screening series. The incidence of positive patch test results to CAPB, cocamide DEA, and amidoamine among patients with AD (n = 242) and without AD (n = 1422) was assessed. Statistical analysis was done using a χ^2 test.

Results: AD was associated with contact hypersensitivity to CAPB, but not to cocamide DEA or amidoamine.

Limitations: This was a retrospective study of patients evaluated for suspected allergic contact dermatitis and, therefore, matching for gender, age, or other parameters was not possible. Our population was geographically limited to metropolitan Kansas City, MO, and metropolitan New York City, NY.

Conclusions: Patients with AD should avoid the use of skincare products containing the surfactant CAPB. (J Am Acad Dermatol <http://dx.doi.org/10.1016/j.jaad.2013.12.009>.)

Key words: allergy; atopic eczema; cocamidopropyl betaine; hypersensitivity; patch testing; surfactants.

Atopic dermatitis (AD), synonymous with atopic eczema, is a chronic, inflammatory skin condition that is associated with abnormalities in skin barrier function.¹ Soap and detergents are known aggravators of AD that can exacerbate the breakdown of the skin barrier.^{2,3} In prior reviews of the database used in this study, patients with a history of AD were significantly more likely than nonatopic populations to develop cutaneous delayed-type hypersensitivity to at least 1 allergen on the North American Contact Dermatitis Group (NACDG) standard tray, most significantly to metal allergens⁴ and to formaldehyde releasers.⁵

Abbreviations used:

AD:	atopic dermatitis
CAPB:	cocamidopropyl betaine
DEA:	diethanolamide
DMAPA:	dimethylaminopropylamine
NACDG:	North American Contact Dermatitis Group
SLES:	sodium laureth sulfate

As a follow-up to these prior findings, we wanted to investigate whether patients with AD are more likely to have an allergic reaction to the detergents

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cocamidopropyl betaine (CAPB) and cocamide DEA, or to the surfactant precursor amidoamine, all of which have been tested on the NACDG standard tray since 2001.

METHODS

This is a retrospective study of 1674 patients evaluated for suspected allergic contact dermatitis between January 1, 2001 (when CAPB, amidoamine, and cocamide DEA were added to the NACDG standard tray), and June 3, 2013. All patients underwent patch testing to the NACDG standard allergen series by the senior author in metropolitan Kansas City, MO, and New York, NY. Patients were not matched for age, gender, or other parameters.

Before patch testing, all patients completed a standardized questionnaire regarding demographic, medical, and occupational data. Atopic status (dermatitis, asthma, hay fever) was assessed in all patients. The diagnosis of AD was established using the criteria of Hanifin and Rajka.⁶

Patients were patch tested in a standardized manner using Finn Chamber (SmartPractice, Phoenix, AZ) on Scanpor tape (Bard Medical, Covington, GA).⁷ Patch tests were applied to areas of the back free of dermatitis. In general, patients with active dermatitis involving 25% or more of body surface area were not patch tested because of the enhanced possibility of false-positive (“angry back”) reactions. Test allergens were purchased from Chemotechnique Diagnostics AB, Malmö, Sweden (2001-2007) or from SmartPractice, Calgary, Alberta, Canada (2008-2013). Allergens were applied on Mondays, and patients were examined at days 2 and 4 after placement. Reactions were assessed based on morphology as previously described.³ Reactions scored as 1+, 2+, or 3+ were considered a positive allergic response.

All deidentified Health Insurance Portability and Accountability Act—compliant data were entered, retrieved, and evaluated using a computer database (Access 2010, Microsoft Corp, Seattle, WA), and this study was therefore considered exempt from institutional review board approval at Columbia University Medical Center, New York, NY. The incidence of contact sensitization to the surfactants CAPB and cocamide DEA and to the surfactant precursor amidoamine among patients with AD

($n = 252$) and without AD ($n = 1422$) was assessed. A χ^2 test was conducted to test whether the difference between observed and expected frequencies was statistically significant, using statistical software (R, Version 3.0.1, R Foundation for Statistical Computing, Vienna, Austria). For cocamide DEA, statistics were performed to calculate

the sample size needed to detect a significant difference between the atopic and non-atopic populations (Epitools Epidemiological Calculators, AustVet Animal Health Services, South Brisbane, Australia).

RESULTS

Of the 1674 patients patch tested, 15.05% ($n = 252$) had a history of AD. Of the 564 males tested, the incidence of AD was 9.86% ($n = 51$). Among the 1109 females, the incidence of AD was 18.12% ($n = 201$).

There was a significantly higher incidence of positive patch test reactions to CAPB among those persons with a history of AD as compared with the nonatopic population (Fig 1). Subanalysis by gender was not statistically significant, most likely because of the small sample size (Table I). For amidoamine and cocamide DEA, there was no statistically significant difference in the incidence of positive responses between atopic and nonatopic patients; these results held true when analyzed by gender (Table I and Fig 1). Assuming the percentage of atopic patients in the total population (15.05%) remained the same, and the same proportions reacted positively to cocamide DEA, 7457 patients would need to be tested to find a significant difference in positive reactions to cocamide DEA between the atopic and nonatopic groups. Assuming the percentage of females patch tested in the population remained the same (66.25%), and the same proportions reacted positively to cocamide DEA, 10,018 patients (consisting of 6637 females) would need to be tested to detect a significant difference ($P < .05$) in positive reactions to cocamide DEA between female patients with and without AD.

In the total population we studied ($n = 1674$), 39 patients reacted positively to CAPB (2.33%), 22 reacted positively to amidoamine (1.31%), and 28 reacted positively to cocamide DEA (1.67%). Five of the patients who reacted positively to CAPB concomitantly reacted positively to amidoamine.

CAPSULE SUMMARY

- Atopic individuals have abnormalities in skin barrier function and are predisposed to developing cutaneous delayed-type hypersensitivity.
- Atopic individuals were significantly more likely to exhibit cutaneous delayed-type hypersensitivity to the surfactant cocamidopropyl betaine, but not to cocamide DEA or amidoamine.
- Atopic patients should minimize cutaneous contact with products that contain cocamidopropyl betaine.

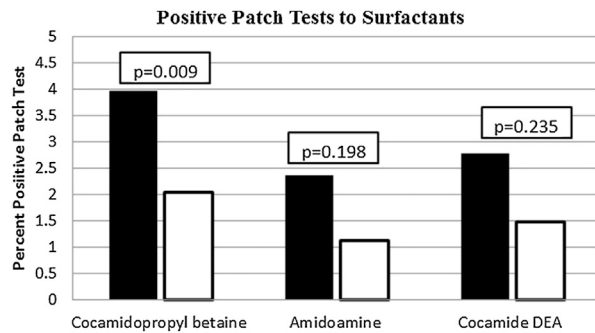


Fig 1. Cutaneous delayed-type hypersensitivity to the surfactants of interest among patients with atopic dermatitis (*solid bars*) and those without (*open bars*).

Table I. Detergents and their rates of positive patch test results among atopic and nonatopic populations, stratified by gender

	Atopic eczema positive		Atopic eczema negative		P value
	No.	%	No.	%	
Cocamidopropyl betaine	10/252	3.97	29/1422	2.04	.009
Female	7/201	3.48	17/908	1.87	.264
Male	3/51	5.88	12/513	2.34	.322
Amidoamine	6/252	2.38	16/1422	1.13	.198
Female	5/201	2.49	10/908	1.10	.239
Male	1/51	1.96	6/513	1.17	1.000
Cocamide DEA	7/252	2.78	21/1422	1.48	.235
Female	6/201	2.99	15/908	1.65	.347
Male	1/51	1.96	6/513	1.17	1.000

Four of the patients who reacted positively to CAPB concomitantly reacted positively to cocamide DEA. Patients who reacted positively to CAPB were significantly more likely to react positively to amidoamine, and to cocamide DEA, than were patients who did not have a positive reaction to CAPB (Fig 2).

DISCUSSION

This was a retrospective study of patients who underwent patch testing for suspected allergic contact dermatitis. As such, patients could not be matched for age, gender, or other parameters. However, our finding that 15.05% of our patients had a history of AD is consistent with data from the United States,⁸ suggesting that we did not have a selection bias for or against patch testing patients with AD. Furthermore, the higher number of females (18.12%) than males (9.86%) presenting with AD has previously been noted by Odhiambo et al,⁹ especially among older patient populations, such as ours. Nonetheless, in the absence of being able to

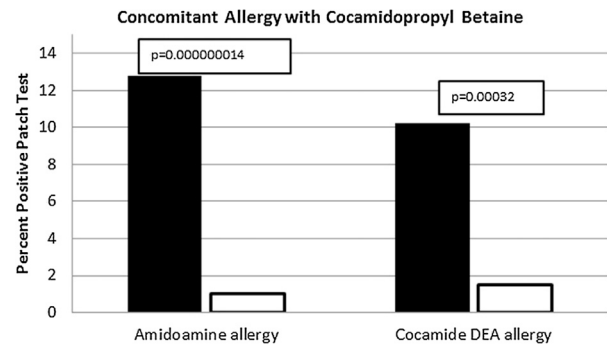


Fig 2. Cutaneous delayed-type hypersensitivity to amidoamine and cocamide DEA among patients with positive reactions to cocamidopropyl betaine (*solid bars*) and those without (*open bars*).

fully match the atopic and nonatopic populations, it is possible that confounding variables other than AD may have influenced our results.

Patients with AD are known to have impaired skin function^{1,2,10-13} that manifests with a weakened barrier, increased water loss, and a lower threshold for the activation of inflammation.¹¹ Cleansing agents expose skin to irritants, which, after repeated use, can potentially damage the skin.^{14,15} Soap and detergents are known aggravators of AD that further contribute to the breakdown of the already impaired skin barrier.^{2,3}

After repeated use, soaps and detergents can rarely cause allergic contact dermatitis in addition to irritant contact dermatitis.¹⁶ Irritant contact dermatitis disrupts the skin barrier and allows increased penetration of allergenic substances. Thus, pre-existing irritation, which occurs more frequently in atopic patients, can contribute to the development of allergic contact dermatitis.¹⁷

The surfactant CAPB is frequently used in personal hygiene and cosmetic products. Major known impurities of CAPB include low quantities of dimethylaminopropylamine (DMAPA), a starting material for formation of CAPB, and amidoamine, an intermediate in the formation of CAPB.^{18,19} There is debate over whether the real allergen in cases of allergic contact dermatitis to CAPB is the product itself, or the impurities DMAPA and amidoamine.^{16,18-22} The detergent cocamide DEA is frequently used in shampoos, hand gels, liquid soaps, and dishwashing liquids. It rarely causes allergic contact dermatitis.^{16,23}

Our data show that persons with a history of AD are significantly more likely than the nonatopic dermatitis population to have a positive allergic patch test reaction to the detergent CAPB. This finding of an increased incidence of cutaneous delayed-type hypersensitivity in atopic patients is consistent with the previous findings

of Schnuch et al.¹⁸ Our study finds no significant difference in the prevalence of allergic reactions to cocamide DEA or amidoamine between the atopic and nonatopic populations, although there was a trend, especially in females with AD, that, had our patch tested population been larger (n = 10,018), would have reached significance.

Patients allergic to CAPB were significantly more likely to react to amidoamine than patients who were not allergic to CAPB. In the 5 patients who were allergic to both CAPB and amidoamine, the CAPB allergy could potentially be attributed to traces of amidoamine in the CAPB patch testing materials. However, 17 patients were allergic to amidoamine and not CAPB and 34 patients were allergic to CAPB and not amidoamine. In these patients, we are unable to comment on the role of DMAPA in the allergic responses because this allergen was not added to the NACDG standard tray until 2009. We therefore did not have sufficient sample size to analyze allergic responses to DMAPA. Our data showed that patients who reacted to CAPB were significantly more likely to react to cocamide DEA than patients who did not react to CAPB. Cross-reactions or common metabolites between the 2 are unlikely (written communication, Daniel C. Liebler, PhD, July 9, 2013).

In summary, our patients with AD were more likely to have a cutaneous delayed-type hypersensitivity reaction to CAPB than those without AD. We did not find atopics to be significantly more likely to react to amidoamine or cocamide DEA than nonatopics, although there was a trend, especially in females with AD. Based on our findings, we recommend that health care practitioners counsel their atopic patients to minimize cutaneous contact with personal care products containing these surfactants. Sodium laureth sulfate (SLES), not to be confused with sodium lauryl sulfate, is another surfactant used in many cleansing agents. When evaluated by the Cosmetic Ingredient Review Expert Panel, it was found to rarely cause dermal irritation, but not sensitization.^{24,25} Considering the reports that SLES is a mild and rare irritant and not a sensitizer,²⁴⁻²⁶ and the lack of reports of SLES sensitization in the literature, we believe that cleansers containing the surfactant SLES would be a safer alternative for the atopic population than products containing CAPB and cocamide DEA.

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