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Patients with Patch Test Reactions Associated with Eye Care Products: Retrospective Analysis of North American Contact

Dermatitis Group Data, 2001-2018

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Eye care products (ECP) may cause allergic contact dermatitis (ACD).

Methods

This ethics-approved study employed standard North American Contact Dermatitis Group (NACDG) methodology.¹ ECPs were defined as over-the-counter (OTC) eye drops/ointments, lid care products, and contact lens solutions. Patients tested by the NACDG (2001-2018) with ≥ 1 positive patch test reaction associated with an ECP comprised the ECP-positive group. Irritant contact dermatitis (ICD) to ECPs was considered separately.

Results

154/43,722 patients (0.4%) had ≥ 1 positive patch test reaction attributed to an ECP. ECP-positive patients had significantly greater odds of female sex, age >40 years old, or history of hay fever (Table 1). When up to 3 anatomic sites were considered, all ECP-positive patients had facial involvement (Table 2).

53.9% of ECP-positive patients (83/154) had 99 total reactions to NACDG screening allergens; the remainder (n=71) had reactions to allergens/substances not on the screening series. The top NACDG screening allergens present in ECPs were thimerosal

(47.8%, 45.5% current relevance [CR]), benzalkonium chloride (BAC) (26.1%, 100% CR); oleamidopropyl dimethylamine (7.7% ,100% CR), propylene glycol (7.1%, 100% CR), ethylenediamine dihydrochloride (4.8%, 100% CR), and lanolin (4.6%, 100% CR). There were no occupationally relevant ECP-associated reactions.

64 patients had ICD due to ECPs; 5 of these had both ICD and ACD due to ECPs.

Discussion

From 2001-2018, 0.4% of 43,722 patients had a positive patch test attributed to an ECP. ECP-positive patients had greater odds of female sex, age >40 years, and/or had a history of hay fever. This correlates with the findings that two-thirds of contact lens wearers are female,² dry eye prevalence increases with age and female gender,³ and seasonal allergic conjunctivitis is commonly treated with OTC antihistamine-containing ECPs. As expected, ECP-positive patients commonly had primary involvement of eyelid (46.1%) or conjunctiva/eye (7.1%), similar to frequencies of a German study (n=118) of 64.4% and 6.8%, respectively.⁴

Here, 64 patients had ICD due to ECPs, 59 of those without co-existing ACD. A Belgian study found that 7.6% (9/118) of patients with positive patch test reactions to ingredients in OTC/prescription ophthalmic medications also had ICD.⁵

Specific allergens associated with ECPs are limited in this dataset. The two most common preservatives (BAC and thimerosal) were only tested in the screening series for 2/18 years; there were only 9 reactions associated with ECPs from 2015-2018. BAC is the most commonly used preservative in eye drops.⁶ In Europe, positivity to BAC associated with eye drops is estimated to be 1.1%.⁵ A recent ingredient analysis of US products found that roughly one-third of top selling OTC eye lubricants contained BAC; other

common allergens were propylene glycol, sorbic acid, amidoamine and sorbitan sequeioleate.⁷ Reactions to benzalkonium chloride should be interpreted carefully due to its propensity to cause irritation when patch tested.⁸ Prior to the 1980s, thimerosal was an important ophthalmic preservative.⁹ Now in the U.S, it is less commonly used – no contact lens or topical ECPs contain thimerosal in the ACDS CAMP database.¹⁰

Additional allergens included oleamidopropyl dimethylamine (7.7%), propylene glycol (7.1%), and lanolin (4.6%), all of which may cause ACD.^{11,12}

46.1% of ECP-positive patients had ≥ 1 positive patch test reaction to a supplemental allergen/substance associated with an ECP source. Names of supplemental allergens are not recorded but our recollection is that the vast majority were due to BAC after it was removed from the screening series, as the frequency of patients with ECP-related supplemental reactions increased significantly after the 2001-2002 cycle (4.2% vs. 12.0%).

In summary, 0.4% of NACDG patients had ECP allergy. Benzalkonium chloride was both common and clinically relevant. Over 46% of patients would have had ≥ 1 positive patch test reaction missed if only tested to the NACDG screening series.

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Table 1. MOAFHLA			
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	ECP+ No. (%) (N = 154)†	ECP- No. (%) (N = 43509)†	OR (95% CI), P value
MOAHFLA			
Male	28 (18.2)	14085 (32.4)	0.46 (0.31-0.77) <0.0001
Occupationally related	5 (3.2)	5046 (11.6)	0.25 (0.11-0.60) 0.0004
Atopy			
Hay fever	62 (40.3)	13037 (30.0)	1.57 (1.13-2.15) 0.0080
Eczema	37 (24.0)	10720 (24.6)	0.96 (0.66-1.10) 0.9255
Asthma	20 (13.0)	6725 (15.5)	0.81 (0.51-1.28) 0.4360
Hand (primary)	11 (7.1)	9875 (22.7)	0.26 (0.14-0.48) <0.0001
Leg (primary)**	1 (0.6)	1783 (4.1)	0.15 (0.02-0.87) 0.0230
Face (primary)* **	123 (79.9)	12774 (29.4)	9.53 (6.41-14.11) <0.0001
Age, 40 > y	120 (77.9)	24428 (56.1)	1.74 (1.20-2.56) 0.0034

*Face includes face (generalized), nose, lips, eyes, eyelids, and face (not otherwise specified)

** As primary site

† Available data varied slightly for demographic variables (eye care product negative: sex, 25 missing; age, 54 missing; hay fever, 154 missing, atopic dermatitis, 199 missing; asthma, 158 missing; primary anatomic sites, 64 missing; occupational relevance, 158 missing)

Table 2. Anatomic Site(s)

	Primary Site			Primary and Non-Primary Sites*		
	ECP Positive No. (%) N = 154	ECP Negative No. (%) N = 43509	OR (95% CI) P value	ECP Positive No. (%) N = 154	ECP Negative No. (%) N = 43509	OR (95% CI) P value
Face, total	123 (79.9)	12774 (29.4)	9.53 (6.41-14.11) <0.0001	167 (1.08)	17514 (40.3)	>100 (71.81 to >100) <0.0001
Eyelids	71 (46.1)	3774 (8.7)	8.99 (6.50-12.33) <0.0001	89 (57.8)	4711 (10.8)	11.26 (8.20-15.50) <0.0001
Face, not otherwise specified	38 (24.7)	6765 (15.5)	1.78 (1.22-2.57) 0.0019	57 (37.0)	9462 (21.7)	2.11 (1.53-2.92) <0.0001
Eyes	11 (7.1)	203 (0.5)	16.4 (9.00-30.02) <0.0001	11 (7.1)	356 (0.8)	9.31 (5.12-16.80) <0.0001
Lips	2 (1.3)	1580 (3.6)	0.35 (0.08-1.24)	7 (4.5)	2088 (4.8)	0.94 (0.44-1.97)

			0.1214			0.8800
Ears	1 (0.6)	430 (1.0)	0.65 (0.06-3.63) 0.6699	2 (1.3)	839 (1.9)	0.67 (0.16-2.38) 0.5689
Nose	0 (0.0)	22 (0.05)	0.00 (0.00-44.18) 0.7800	1 (0.6)	58 (0.1)	4.89 (0.48-26.41) 0.0822
Hand	11 (7.1)	9875 (22.7)	0.26 (0.14-0.48) <0.0001	17 (11.0)	11622 (26.7)	0.34 (0.21-0.55) <0.0001
Scattered generalized	10 (6.5)	7957 (18.3)	0.31 (0.16-0.57) <0.0001	23 (14.9)	9847 (22.6)	0.60 (0.38-0.93) 0.0205
Scalp	4 (2.6)	1485 (3.4)	0.75 (0.30-1.90) 0.8225	8 (5.2)	2396 (5.5)	0.94 (0.45-1.84) >0.99
Other Sites †	2 (1.3)	2014 (4.6)	0.27 (0.07-1.00) 0.0513	4 (2.6)	2500 (5.7)	0.45 (0.17-1.12) 0.1153
Trunk	1 (0.6)	2413 (5.5)	0.11 (0.01-0.65) 0.0038	10 (6.5)	5362 (12.3)	0.49 (0.29-0.93) 0.0263
Leg	1 (0.6)	1783 (4.1)	0.15 (0.02-0.87) 0.0230	7 (4.5)	4655 (10.7)	0.40 (0.19-0.82) 0.0122
Anal/genital	1 (0.6)	908 (2.0)	0.31 (0.03-1.69) 0.3858	3 (1.9)	1269 (2.9)	0.66 (0.22-1.92) 0.6337

Neck	1 (0.6)	788 (1.8)	0.35 (0.04-28.42)	16 (10.4)	3844 (8.8)	1.19 (0.70-1.99)
			0.5346			0.4769
Arm	0 (0.0)	2114 (4.9)	0.0 (0.0-0.44)	5 (3.2)	6546 (15.0)	0.22 (0.10-0.49)
			0.0010			<0.0001

*percentages for all sites >100% because up to 3 sites could be recorded

**Available data varied slightly (eye care product negative primary anatomic sites, 64 missing)

^ap value calculated using Fisher's exact test

† includes most exposed areas, only under clothing, foot, ears, erythroderma and Other, NOS