

Cosmetic dermatitis in Chinese eczema patients patch tested with a modified European standard series of allergens

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The prevalence of cosmetic allergic contact dermatitis (CACD) in Chinese eczema patients (CEP) has not been reported. The purpose of our study was to analyse CACD in CEP and examine the frequency of patch test (PT) reactions to common cosmetic-related allergens (CRA). 378 consecutive CEP patch tested with a modified European standard series of allergens during a 2-year period in our clinic were analysed. 73 patients (19.3%) were considered as suspected CACD and 37 patients (9.8%) were confirmed. The frequencies of the positive PT reactions in suspected CACD and confirmed CACD to at least 1 CRA were 64.4% and 89.2%, to para-phenylenediamine (PPD) were 31.5% and 59.5%, to fragrance mix (FM) were 27.4% and 32.4% and to imidazolidinylurea were 5.5% and 8.1%, respectively. These results were much higher than those of CEP without cosmetic reactions (26.3% for at least 1 CRA, 5.8% for PPD, 8.8% for FM, and 0 for imidazolidinylurea) ($P < 0.01$ for all, Chi-square test and Fisher's exact test). These results suggested that CACD is very common in CEP patch tested. PPD and FM are the leading allergens identified. CACD should be strongly considered in CEP with positive PT reactions to PPD, FM and imidazolidinylurea.

Key words: allergic contact dermatitis; Chinese; cosmetics; fragrance mix; para-phenylenediamine; patch test; prevalence. © Blackwell Munksgaard, 2005.

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Cosmetics are widely used to enhance the physical, mental and spiritual well-being of mankind. Increasing use of cosmetics by modern society has contributed to rising in the incidence of cosmetic allergic contact dermatitis (CACD). Of eczema patients patch tested in the 1980s, about 4–6% of the patients were allergic to cosmetics (1, 2). However, it has increased to 8–15% since 2000 (3–5).

The prevalence of CACD in Chinese eczema patients (CEP) has not been reported. The purpose of this study was to investigate CACD in CEP and examine the frequency of patch test (PT) reactions to common cosmetic-related allergens (CRA). 378 consecutive CEP patch tested with European standard series of allergens during a 2-year period in Peking University Third Hospital, Beijing, China were analysed.

Patients and Methods

Diagnostic criteria

Eczema. Eczema was diagnosed by clinical manifestations according to standard textbooks (6, 7).

Specific types of eczema, such as contact dermatitis, atopic dermatitis, asteatotic eczema and seborrhoeic dermatitis, were clinically diagnosed accordingly (6, 7), and the remaining unspecified eczema was diagnosed as unclassified eczema.

CACD. CACD was suspected by the disease history and clinical examination based on a standard textbook (6); only patients with strong evidence supporting the diagnosis were included. If the patients with reported CACD could reapply the suspected cosmetics without any reactions, CACD was excluded.

CACD was confirmed if patients with suspected CACD also fulfil the following criteria (i) positive usage test and/or (ii) positive PT results with the suspected cosmetics as is, or (iii) positive repeated open application test. Because Chinese regulations do not require that cosmetic manufacturer list ingredients on their products and most Chinese cosmetics without ingredient labelling, we could not confirm the CACD so far by a positive PT result to ingredient presented in cosmetics in China.

Cosmetic irritant contact dermatitis (CICD). CICD was diagnosed by the disease history and clinical examination based on standard textbooks (6, 7).

Study population

378 consecutive eczema patients patch tested with European standard series of allergens were studied. All patients were from our dermatology clinics during the period between July 2001–February 2002 and June 2002–February 2003. There were 120 males and 258 females, with an average age of 40.5 ± 16.4 years (mean $\pm$ SD). The average course of dermatitis was 35.6 ± 63.4 months (mean $\pm$ SD).

Patch testing

Patch testing was performed with a modified European standard series of allergens (Chemotechnique Diagnostics, Malmö, Sweden) (Table 1). Among them, 2-bromo-2-nitropropane-1,3-diol, colophony, formaldehyde, fragrance mix (FM), imidazolidinylurea, parabens, para-phenylenediamine (PPD), sesquiterpene lactone mix and thimerosal are CRA. Allergens were applied to the upper back, using IQ Chambers (Chemotechnique Diagnostics) for 2 days, and the results were recorded at 2 and 3 days according to ICDRG recommendations (7). If the patient could supply the suspected

cosmetics, patch testing with the patients' own products was also performed, using published methods (7).

Statistical analysis

2 $\times$ Chi-square test or, if appropriate, Fisher's exact test, was used to compare the positivity rate to each allergen in each group. One logistic regression analysis was used to compare the demographic characteristics of each group of patients. A *P*-value <0.05 was regarded as significant (8). The software used was from SPSS (Systat version 11.5, SPSS, Chicago, IL, USA).

Results

Prevalence of CACD

Disease history revealed that 138 (36.5%) of the 378 eczema patients claimed present or past cosmetic reactions. Of the 138 patients, 65 patients could reapply the suspected cosmetics without any reactions, and hence they were excluded from suspected CACD. 73 (19.3%) of the patients were considered as suspected CACD. 45 (11.9%) patients had present suspected CACD and the other 28 patients had suspected CACD in the past. CACD could be confirmed in 37 (9.8%) of the patients; 20 (5.3%) of these had present CACD and the other 17 patients had confirmed CACD in the past. Among the 20 present CACD patients, 4 patients were confirmed by positive patch tests, with the responsible cosmetic product as is; in the other 16 patients, the diagnosis was made by use tests and/or repeated open application tests. 8 (2.1%) patients had present CICD.

Causative cosmetics in CACD

Among the patients with suspected CACD, skin care products accounted for about half (36/73, 49.3%), followed by colour decorating cosmetics (28/73, 38.4%). The most common cosmetics identified was hair dye (24/73, 32.9%), followed by facial cream (23/73, 31.5%), mask (4/73, 5.5%), facial cleansing lotion (3/73, 4.1%) and depigmentation cream (3/73, 4.1%) (Table 2).

Among the patients with confirmed CACD, colour decorating cosmetics accounted for more than half (25/37, 67.6%), followed by skin care products (13/37, 35.1%). The most common cosmetics identified was hair dye (23/37, 62.2%), followed by facial cream (8/37, 21.6%) (Table 2).

Among 8 patients, CICD was caused by facial creams in 6, by facial cleansing lotion in 1 and by hair care product in 1.

Table 1. Allergens in standard series

Allergens	Vehicle	Concentration (%)
Benzocaine	Petrolatum (pet.)	5.0
Black rubber mix	Pet.	0.6
2-Bromo-2-nitropropane-1,3-diol*	Pet.	0.25
Carba mix	Pet.	3.0
Colophony*	Pet.	20.0
Epoxy resin	Pet.	1.0
Ethylenediamine dihydrochloride	Pet.	1.0
Formaldehyde*	Aqua (aq)	1.0
Fragrance mix*	Pet.	8.0
Imidazolidinylurea*	Pet.	2.0
Mercapto mix	Pet.	2.0
N-(Cyclohexylthio) phthalimide	Pet.	1.0
Nickel sulfate	Pet.	5.0
Parabens*	Pet.	16.0
Para-phenylenediamine*	Pet.	1.0
Potassium dichromate	Pet.	0.5
Sesquiterpene lactone mix*	Pet.	0.1
Thimerosal*	Pet.	0.1
Thiuram mix	Pet.	1.0
Tixocortol-21-pivatate	Pet.	0.1

*Cosmetic-related allergens

Table 2. The number (%) of cosmetic allergic contact dermatitis (CACD) cases by causative product category

Product category	Suspected CACD (n = 73)	Confirmed CACD (n = 37)
Skin care products	36 (49.3)	13 (35.1)
Facial cream	23 (31.5)	8 (21.6)
Mask	4 (5.5)	2 (5.4)
Eye cream	2 (2.7)	1 (2.7)
Softening lotion	1 (1.4)	0
Facial cleansing lotion	3 (4.1)	1 (2.7)
Body cleansing lotion	2 (2.7)	0
Fancy soap	1 (1.4)	1 (2.7)
Colour decorating products	28 (38.4)	25 (67.6)
Hair dye	24 (32.9)	23 (62.2)
Lipstick	2 (2.7)	1 (2.7)
Eye shadow	1 (1.4)	1 (2.7)
Powder	1 (1.4)	0
Other hair preparations	4 (5.5)	0
Shampoo	1 (1.4)	0
Waving lotion	1 (1.4)	0
Hair fixing lotion	1 (1.4)	0
Hair mask	1 (1.4)	0
Therapeutic products	5 (6.8)	1 (2.7)
Depigmentation cream	3 (4.1)	1 (2.7)
Anti-acne lotion	1 (1.4)	0
Keratose abrading cream	1 (1.4)	0
Perfume	2 (2.7)	1 (2.7)
Sunscreen products	2 (2.7)	0
Total	77*	40*

*Because some CACD patients were caused by more than 1 product, the total of 77 exceeds the number of suspected CACD (73) by 4, and the total of 40 exceeds the number of confirmed CACD (37) by 3.

MOAHLFA index

The MOAHLFA index lists the proportions of certain demographic variables, namely M for male sex, O for occupational causation of dermatitis, A for atopic dermatitis, H, L, F for hand, leg, face as affected site, respectively, and the last A for the proportion of patients aged 40 and above (9).

The MOAHLFA indices of patients with claimed cosmetic reactions, patients with

suspected CACD and patients with confirmed CACD all differed significantly from patients without cosmetic reactions. In particular, men were significantly underrepresented [$P < 0.01$ for all, OR (95% CI) = 0.144 (0.075–0.280), 0.100 (0.037–0.267) and 0.092 (0.026–0.328), respectively, One logistic regression analysis]. Compared with control, more patients were affected in the face [$P < 0.01$ for all, OR (95% CI) = 3.519 (2.067–5.991), 4.315 (2.191–8.497) and 4.344 (1.687–11.187), respectively, One logistic regression analysis] and older patients (40 and above) were overrepresented [$P < 0.01$ for all, OR (95% CI) = 2.141 (1.279–3.582), 2.396 (1.261–4.554) and 7.414 (2.923–18.801), respectively, One logistic regression analysis] (Table 3).

PT results

The frequencies of the positive PT reactions to at least 1 CRA in patients with claimed cosmetic reactions, patients with suspected CACD and patients with confirmed CACD were 45.7%, 64.4% and 89.2%, respectively, which were much higher than that (26.3%) of eczema patients without cosmetic reactions [$P < 0.01$ for all, OR (95% CI) = 2.360 (1.518–3.670), 5.079 (2.905–8.880) and 23.179 (7.897–68.034), respectively, Chi-square test]. PPD (positivity rate 17.4%, 31.5% and 59.5%) and FM (15.9%, 27.4% and 32.4%) were the leading allergens in patients with claimed cosmetic reactions, patients with suspected CACD and patients with confirmed CACD. Compared with eczema patients without cosmetic reactions, patients with claimed cosmetic reactions showed higher positivity rates to PPD [$P < 0.01$, OR (95% CI) = 3.398 (1.694–6.820), Chi-square test], FM [$P = 0.034$, OR (95% CI) = 1.978 (0.004–3.747), Chi-square test], imidazolidinylurea ($P = 0.002$, Fisher's exact test) and parabens ($P = 0.035$, Fisher's

Table 3. The MOAHLFA index of each group patients

	Patients with claimed cosmetic reactions (n = 138)	Patients with suspected CACD (n = 73)	Patients with confirmed CACD (n = 37)	Patients without cosmetic reactions (n = 240) (control)
Male	13 (9.4)*	5 (6.8)**	3 (8.1)***	107 (44.6)
Occupational dermatitis	0	0	0	3 (1.3)
Atopic dermatitis	5 (3.6)	1 (1.4)	1 (2.7)	2 (0.8)
Hand dermatitis	31 (22.5)	15 (20.5)	9 (24.3%)	88 (36.7%)
Leg dermatitis	21 (15.2)	12 (16.4)	8 (21.6)	45 (18.8)
Face dermatitis	84 (60.9)*	47 (64.4)**	21 (56.8)***	70 (29.2)
Age 40+	68 (49.3)*	38 (52.1)**	28 (75.7)***	106 (44.2)

Values are expressed as n (%).

* $P < 0.05$, patients with cosmetic reactions versus patients without cosmetic reactions.

** $P < 0.05$, patients with suspected CACD versus patients without cosmetic reactions.

*** $P < 0.05$, patients with CACD versus patients without cosmetic reactions.

exact test); patients with suspected CACD showed higher positivity rates to PPD [$P < 0.01$, OR (95% CI) = 3.398 (3.573–15.434), Chi-square test], FM [$P < 0.01$, OR (95% CI) = 3.935 (1.990–7.783), Chi-square test] and imidazolidinylurea ($P = 0.003$, Fisher's exact test); patients with confirmed CACD also showed higher positivity rates to PPD ($P < 0.01$, Fisher's exact test), FM ($P < 0.01$, Fisher's exact test) and imidazolidinylurea ($P = 0.002$, Fisher's exact test) (Table 4).

Among 8 CACD patients, 7 patients had negative PT results to CRA, 1 patient had positive reaction to thimerosal. 2 patients had negative PT results to the suspected cosmetics as is; they also had negative standard PT results.

In addition, FM sensitivity accounted for 34.8% (8 cases) of 23 suspected facial cream allergy patients and 75% (6 cases) of 8 confirmed (Table 2). PPD sensitivity accounted for 91.7% (22 cases) of 24 suspected hair dye allergy patients and 95.7% (22 cases) of 23 confirmed (Table 2).

Discussion

Our results showed that 138 (36.5%) of 378 consecutive CEP reported cosmetic reactions, indicating cosmetics were commonly blamed in CEP. Clinical analysis and PT revealed 73 (19.3%) of the patients having suspected CACD and 37 (9.8%) of the patients being confirmed. These results were similar to literatures reported recently (3–5), suggesting that although China is a developing country, CACD in eczema patients is also very common and should be detected.

In our case, only 8 (2.1%) of the patients had present CACD, which was much fewer than

CACD. It is reported that irritant reactions to cosmetics occur much more common than allergic reactions in general population, and more than 90% of adverse reactions to cosmetics are due to irritation (10). Fewer CACD in our study may be due to irritant reactions are usually mild and many patients do not go for a doctor and be patch tested.

It has been reported that skin care products accounted for 29.2% of 601 cosmetic sensitization (1985, USA) (1) and 52.3% in 75 cosmetic allergy patients (1987, Netherlands) (2). Facial cream allergy was reported in 14% of 50 suspected CACD patients (2000, India) (3) and in 32.4% among 53 suspected allergic contact eczema/dermatitis (ACED) from cosmetic usage (2002, Spain) (4). The prevalence of skin care product sensitivity in our CACD patients was in consistent with other reports, indicating that skin care products are also very important in Chinese CACD. Compared with other reports, hair dye sensitization in our case was very higher, which was only 7.5% (1985, USA) (1) and 26.4% (2002, Spain) (4). However, similar prevalence of hair dye allergy (62%) has been reported in India (3).

The PT results of patients with claimed cosmetic reactions, patients with suspected CACD and patients with confirmed CACD showed that PPD (17.4%, 31.5% and 59.5%, respectively) and FM (15.9%, 27.4% and 32.4%, respectively) were leading allergens (Table 4). It has been reported that FM allergy frequency was ranged from 44.1% in 53 patients with suspected cosmetic dermatitis (2002, Spain) (4) to 79% in 29 cosmetic-related dermatitis (2000, UK) (11). The most common allergen reported in 50 suspected CACD patients in India in 2000 was fragrance also (47%) (3). PPD allergy was found in 23.5% among 50 suspected CACD patients (2000, India)

Table 4. The positive number (%) on patch testing of each group patients

Cosmetic-related allergens	Patients with claimed cosmetic reactions ($n = 138$)	Patients with suspected CACD ($n = 73$)	Patients with confirmed CACD ($n = 37$)	Patients without cosmetic reactions ($n = 240$) (control)
Total (reacted to at least 1 cosmetic-related allergen)	63 (45.7)*	47 (64.4)**	33 (89.2)***	63 (26.3)
Bronopol	2 (1.4)	2 (2.7)	1 (2.7)	3 (1.3)
Colophony	4 (2.9)	3 (4.1)	2 (5.4)	12 (5.0)
Formaldehyde	6 (4.3)	5 (6.8)	1 (2.7)	6 (2.5)
Fragrance mix	22 (15.9)*	20 (27.4)**	12 (32.4)***	21 (8.8)
Imidazolidinylurea	6 (4.3)*	4 (5.5)**	3 (8.1)***	0 (0)
Parabens	8 (5.8)*	3 (4.1)	1 (2.7)	4 (1.7)
Para-phenylenediamine	24 (17.4)*	23 (31.5)**	22 (59.5)***	14 (5.8)
Sesquiterpene lactone mix	1 (0.7)	1 (1.4)	1 (2.7)	4 (1.7)
Thimerosal	12 (8.7)	6 (8.2)	3 (8.1)	17 (7.1)

* $P < 0.05$, patients with cosmetic reactions *versus* patients without cosmetic reactions.

** $P < 0.05$, patients with suspected CACD *versus* patients without cosmetic reactions.

*** $P < 0.05$, patients with CACD *versus* patients without cosmetic reactions.

(3) and in 23% of 53 suspected allergic contact eczema/dermatitis from cosmetic usage (2002, Spain) (4). Compared with these reports, PPD sensitivity was relatively higher and FM sensitivity was relatively lower in our case. The wider use of black hair dyes and less frequent use of perfumes, deodorants and other aroma products in China may be possible reasons. In central Europe, a steady decline from 27.6% to 17.2% in PPD contact allergy was observed in female hairdressers, while a significant increase was noted in female clients (12.6% and 16.6% in 1995/1996 and 2001/2002, respectively) (12). A significant decline in sensitization to the FM has been reported for the first time in Europe, in which a significant increase in the proportions of patients with positive reactions to FM between 1996 and 1998 is noted and a significant decline in from 1999 to 2002. The highest frequency of sensitization to FM was 13.1% in 1999 and the lowest was 7.8% in 2002. The authors think that the significant decrease is probably due to reduced exposure (less potent allergens used in fine fragrances, possibly less use of natural ingredient-base cosmetics and less use of important fragrance allergens) (13).

Compared with patients without cosmetic reactions ever, three groups of patients all showed higher positivity rates to PPD, FM and imidazolidinylurea (Table 4). These results indicated that CACD should be strongly considered in CEP with positive PT reactions to PPD, FM and imidazolidinylurea.

PPD is the most commonly used hair dye allergy marker in patch testing. Fabric or leather dye, rubber and plast are other common non-cosmetic PPD sensitization origins. In our case, 22 of 38 PPD-sensitive patients were hair dye allergic (Table 4), suggesting that hair dye allergy was the main cause in our PPD-sensitive patients. In addition, 22 of 24 suspected (23 confirmed) hair dye allergy patients were PPD sensitive, indicating PPD is the main allergen in hair dyes in China, although it has been reported that some hair dye substances were used in higher tonnage and had higher predicted sensitization potential in Europe (14). A statistically significant difference in the sensitization rate for PPD in blacks compared with whites has been reported (15), which may due to more blacks dyeing their hair black.

FM is commonly used in cosmetic products, as well as in traditional Chinese medicine (TCM). Chemical analysis has revealed that well-known allergens from the FM are present in 15–100% of cosmetic products and most often in combinations of three to four allergens in the same

products (16). In our study, higher FM sensitivity was found in CACD patients than patients without cosmetic reactions, indicating that FM sensitization was mainly cosmetic related in CEP. In 21 FM-positive patients without cosmetic reactions, 13 patients (61.9%) were allergic to TCM; the relevance of positive PT reaction in the other 8 patients was uncertain.

Imidazolidinylurea is a well-known sensitizer, which is commonly used in cosmetic products as well as in external drugs. Our results implicate that imidazolidinylurea sensitization was mainly cosmetic related in CEP.

The parabens are also preservatives with low sensitization potency. Considering their frequent use in external drug preparations, cosmetics and perioral products, the overall sensitization rate can be regarded as low. Our results were comparable to other reports (Table 4). 1.6% has been reported in 28 349 patients tested with preservatives of the standard series (SS) in IVDK in 1990–1994 (17), 1.09%, 2.64% and 4.27% has been reported in IVDK in three age groups: ≤ 60 , 61–75 and ≥ 76 years (18). 12.1% of parabens positivity has been reported in 53 suspected allergic contact eczema/dermatitis (ACED) from cosmetic usage (2002, Spain) (4). In our study, higher frequency of parabens sensitization was found in patients with claimed cosmetic reactions; however, it was of no significant difference in patients with suspected CACD and confirmed CACD (Table 4). It is generally believed that parabens allergy increases with age; older patients were overrepresented in our patients with claimed reactions (Table 3).

No significant differences were found in the positivity rates of the other 5 CRA (2-bromo-2-nitropropane-1,3-diol, colophony, formaldehyde, sesquiterpene lactone mix and thimerosal) between patients with or without CACD (Table 3). These results indicate that positive PT reactions to these allergens were not mainly cosmetic related in CEP. A study of 24 departments participating in the Information Network of Departments of Dermatology in Germany during 1990–1994 showed there were high (and significant) percentages of patients from the medical and paramedical professions in thimerosal-positive patients and formaldehyde-positive patients, indicating patients with positive reactions to the two allergens were occupational related (17). Increased use of new vaccines such as hepatitis B vaccine or tick-borne encephalitis vaccine preserved by thimerosal was considered as one cause of thimerosal sensitization (17).

In summary, our results showed that CACD is also very common in China. The most common cosmetics causing suspected CACD is facial

cream, while the most common cosmetics confirmed is hair dye. The most common allergens in CACD are PPD and FM. We appeal that the supervisor of PPD in hair dyes should be strengthened promptly in China. CACD should be strongly considered in CEP with positive PT reactions to PPD, FM and imidazolidinylurea. PT with European standard series of allergens is very valuable in screening CACD in CEP.

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