

Patch test in Chinese patients with cosmetic allergic contact dermatitis to common cosmetic allergens from a European cosmetic series

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Lin-Feng Li, Guangren Liu and Jing Wang

Department of Dermatology, Peking University Third Hospital, Beijing 100083, China

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The incidence of cosmetic allergic contact dermatitis (CACD) in patients with eczema patch tested has increased to 8–15% in 2000s (1–3). China is the biggest developing country in the world, with the development of economics, more and more Chinese use cosmetics especially those imported from developed countries. In 2005, we had reported the prevalence of CACD in Chinese eczema patients (CEPs) was 9.8% (4). In that study, CEPs were only patch tested with a modified European standard series of allergens. The patch test (PT) reactions of Chinese CACD to common cosmetic series of allergens have not been reported in China. The purpose of this study was to examine the frequency of PT reactions to common cosmetic allergens (CCAs) in Chinese patients with CACD. A total of 655 consecutive

patients with eczema patch tested with a modified European standard series and 20 of 48 CCA from a European cosmetic series during a 2-year period in Peking University Third Hospital, Beijing, China, were analyzed.

Patients and Methods

A total of 655 consecutive CEPs patch tested in the Department of Dermatology, Peking University Third Hospital, from September 2003 to May 2005 were studied. CACD was suspected by the disease history, and clinical examination based on standard textbooks (5, 6). If the patients with suspected CACD could reapply the suspected cosmetics without any reactions, CACD was excluded. CACD was confirmed in patients with (i) positive usage test and/or (ii) positive PT result 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 labeling, we could not confirm the CACD by a positive PT result to ingredient presented in cosmetics in China.

Patch testing was performed with a modified European standard series and CCAs selected from a European cosmetic series (Chemotechnique Diagnostics, Malmö, Sweden) (Table 1). For the economic reason and convenience, only 20 of total 48 CCAs were selected. 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 the International Contact Dermatitis Research Group recommendations (6). If possible, patch testing with the patients' own products was also performed (6). The suspected causal agent was investigated using a questionnaire after patch testing (7). In the questionnaire, patient's personal data; present illness (patients' description, date of onset, effects of weekends, effects of vacation, and previous therapy); contactants existed in work, clothes, toiletries, household, and treatment; atopic diathesis; and medications (taking presently or within last 3 months) were included. Patients were followed up for 3 months to further confirm the diagnosis. If the dermatitis recurred in patients with suspected CACD after re-exposure to the suspected

Table 1. The standard series and cosmetic series of allergens patch tested

Allergen
Standard series of allergens
Benzocaine
Black rubber mix (IPPD, CPPD, DPPD)
2-Bromo-2-nitropropane-1,3-diol (bronopol)*
Carba mix (1,3-diphenylguanidine, ZDC, ZBC)
Colophonium*
Epoxy resin
Ethylenediamine dihydrochloride
Formaldehyde*
Fragrance mix (cinnamic alcohol, hydroxycitronellal, amylcinnamal, geraniol, eugenol, isoeugenol, oakmoss absolute)*
Imidazolidinyl urea*
Mercapto mix (<i>N</i> -cyclohexylbenzothiazylsulfonamide, mercaptobenzothiazole, dibenzothiazyl disulfide, morpholinylmercaptobenzothiazole)
<i>N</i> -(Cyclohexylthio) phthalimide
Nickel sulfate
4-Phenylenediamine base (PPD)*
Parabens (methyl-4-hydroxybenzoate, ethyl-4-hydroxy benzoate, propyl-4-hydroxy benzoate, butyl-4-hydroxy benzoate)*
Potassium dichromate
Sesquiterpene lactone mix (alantolactone, dehydrocostus lactone, costunolide)*
Thiuram mix (TMTM, TMTD, TETD, PTD)
Thimerosal (merthiolate)*
Tixocortol-21-pivalate
Cosmetic series of allergens†
Abitol
Amerchol L 101
Chlorhexidine digluconate
2-Chloroacetamide
4-Chloro-3,5-xyleneol
4-Chloro-3-cresol
Clioquinol
2,6-Di-tert-butyl-4-cresol
2-Hydroxy-4-methoxybenzophenone
Hexahydro-1,3,5-tris-(2-hydroxyethyl)triazine
Isopropyl myristate
Octyl gallate
Phenyl salicylate 1.0 pet.
Polyoxyethylenesorbitanmonooleate
Propylene glycol
Sorbic acid
Sorbitan monooleate
2-tert-Butyl-4-methoxyphenol
Triclosan
Triethanolamine

CPPD, *N*-cyclohexyl-*N*-phenyl-4-phenylenediamine; DPPD, *N,N*-diphenyl-4-phenylenediamine; IPPD, *N*-isopropyl-*N*-phenyl-4-phenylenediamine; PTD, dipentamethylenethiuramdisulfide; TETD, tetraethylthiuramdisulfide; TMTD, tetramethylthiuramdisulfide; TMTM, tetramethylthiuram-monosulfide; ZBC, zinc dibutyl dithiocarbamate; ZDC, zinc diethyldithiocarbamate.

*Cosmetic-related allergens (CA).

†Only 20 allergens from 48 were tested, and other cosmetic allergens, such as methyl dibromoglutaronitrile, were not studied.

cosmetics, CACD was confirmed. Two chi-squared test or, if appropriate, Fisher's exact test, was used to compare the positivity rate to each allergen in each group. A *P* value less than 0.05 were regarded as significant (8). The software used was from spss (Systat version 11.5; SPSS, Chicago, IL, USA).

Results

Five hundred and ninety-nine of 655 (91.5%) patients finished the study. Among them, 93 (15.5%) patients

had suspected CACD. There were 9 men and 84 women (M: F = 1:9) with an average age of 38.2 ± 14.6 years (mean $\pm$ standard deviation). None of them was atopic. The most commonly involved site was the face (68.8%, 64/93), followed by scalp, face, neck, and upper limbs (14/93) and neck with or without face (10/93). Two hand CACD and three widespread CACD were also found. Forty-eight patients (8%) had confirmed CACD. Thirty-three per cent (16/48) of CACD were confirmed by patch testing the patients with suspected cosmetics 'as is', and the other

32 were diagnosed by re-using the suspected cosmetics. CACD developed in 45 of 93 (48%) patients after visiting beauty shop or beauty center. The patients could neither supply the suspected cosmetics nor were willing to re-try the suspected cosmetics. Therefore, CACD could not be confirmed so far.

Among the patients with suspected CACD, skin care products accounted for 66.7% (62/93), followed by color decorating cosmetics (26/93, 28.0%). Facial cream (30/93, 32.3%), hair dye (20/93, 21.5%), facial cleansing lotion (12/93, 12.9%), mask (10/93, 10.6%)

Table 2. The number (%) of CACD cases by causative product category

Product category	Suspected CACD (n = 93)	Confirmed CACD (n = 48)
Skin care products	62 (66.7)	32 (66.7)
Facial cream	30 (32.3)	19 (39.6)
Mask	10 (10.6)	4 (8.3)
Softening lotion	2 (2.2)	1 (2.1)
Facial cleansing lotion	12 (12.9)	5 (10.4)
Body cleansing lotion	4 (4.3)	1 (2.1)
Fancy soap	4 (4.3)	2 (4.2)
Color decorating products	26 (28.0)	17 (35.5)
Hair dye	20 (21.5)	12 (25.0)
Lipstick	2 (2.2)	2 (4.2)
Eye shadow	3 (3.2)	2 (4.2)
Powder	1 (1.1)	1 (2.1)
Other hair preparations	3 (3.2)	3 (6.3)
Shampoo	1 (1.1)	1 (2.1)
Waving lotion	1 (1.1)	1 (2.1)
Hair fixing lotion	1 (1.1)	1 (2.1)
Therapeutic products	3 (3.2)	2 (4.2)
Depigmentation cream	2 (2.2)	2 (4.2)
Keratose abrading cream	1 (1.1)	0
Sunscreen products	9 (9.7)	4 (8.3)
Total	103*	58*

CACD, cosmetic allergic contact dermatitis.

*Because some patients with CACD were caused by more than one product, the total of 103 exceeds the number of suspected CACD (93) by 10 and the total of 58 exceeds the number of confirmed CACD (48) by 10.

and sunscreen (9/93, 9.7%) were the common causative cosmetics (Table 2).

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, and F for hand, leg, and face as affected site, respectively; and the last A for the proportion of patients aged 40 years and above (9). The MOAHLFA indices of patients with suspected CACD differed significantly from those of patients without cosmetic reactions (Table 3).

Most CCA PT yielded positive results. Compared with patients without cosmetic reactions, patients with suspected CACD showed higher positivity rates to *para*-phenylenedi-

amine (PPD), fragrance mix (FM), Amerchol L 101, and abitol. No significant differences were found in the positivity rates of other CCA between patients with or without CACD (Table 4).

Discussion

We have studied the prevalence of CACD in CEP patch tested with European standard series of allergens in our clinic from 2001 to 2003 (4). In that study, 19.3% of the patients had suspected CACD and 9.8% of the patients being confirmed. These results were quite similar to our current results and were consistent with the recent reported prevalence of 8–15% (1–3), suggesting that although

China is a developing country, CACD in patients with eczema is also very common and should not be ignored.

Similar to that study, the leading causative cosmetics for CACD in this study were still skin care products and color decorating products. The proportion of skin care products in suspected CACD (66.7%) was also higher than the 29.2% in 1985 in USA (10) but close to the 52.3% in 1987 in the Netherlands (11). The different consumption of cosmetics or the different MOAHLFA index may cause the difference.

Facial cream allergy accounted to 32.3% of suspected CACD, which was also consistent with 14% of 50 patients with suspected CACD in 2000 in India (1) and 32.4% of 53 suspected allergic contact eczema/dermatitis from cosmetic usage in 2002 in Spain (2), indicating that skin care products especially facial cream were also very important in Chinese CACD.

Hair dye sensitization in CACD has been reported as low as 7.5% in 1985 in USA (10), 26.4% in 2002 in Spain (2), and as high as 62% in 2000 in India (1). In the current study, the prevalence of hair dye allergy in suspected CACD was dropped to 21.5%. The decrease in hair dye allergy in the current study may be because of the bias of patient collection; however, the increasing knowledge on hair dye allergy and safe use of hair dye may also contribute to the decrease.

In this study, we also showed that the clinical features including the sex predominance and the site involvement were also quite similar to those reported in other countries. Considering more and more Chinese people applying imported cosmetics from Europe, America, or Japan, it is necessary to diagnose the CACD early.

Although CACD could be easily suspected, it was very difficult to diagnose so far in China. In this study, only 48 of 93 (42%) suspected CACD were confirmed. Other 45 patients (48.4%) developed their dermatitis from beauty shop or beauty center; CACD could not be diagnosed by PT the suspected cosmetics as is, and the patients were not willing to re-use the suspected cosmetics. Because Chinese regulations do not require the cosmetic manufactures labeling the cosmetic ingredients in their products, we cannot diagnose CACD by CCA PT.

Table 3. The MOAHLFA index of CACD in each group patients

	Suspected CACD (n = 93), n (%)	Patients without cosmetic reactions (n = 506), n (%)
Male	9 (9.7)*	171 (33.8)
Occupational dermatitis	0	8 (1.6)
Atopic dermatitis	0	14 (2.8)
Hand dermatitis	3 (3.2)*	79 (15.6)
Leg dermatitis	0	5 (1.0)
Face dermatitis	79 (84.9)*	181 (35.8)
Age 40+ (years)	35 (37.6)	226 (44.7)

CACD, cosmetic allergic contact dermatitis.

* $P < 0.01$, chi-squared test.

Table 4. The positive number (%) to each cosmetic allergen in patch testing of suspected patients with CACD

Cosmetic allergens	CACD (n = 93)	Patients without cosmetic reactions (n = 506)
Abitol	11 (11.8)	30 (5.9)*
Amerchol L 101	7 (7.5)	11 (2.2)*
2-Bromo-2-nitropropane-1,3-diol	0	2 (0.4)
2-Chloroacetamide	0	4 (0.8)
4-Chloro-3,5-xyleneol	0	3 (0.6)
4-Chloro-3-cresol	3 (3.2)	5 (1.0)
Chlorhexidine digluconate	3 (3.2)	21 (4.2)
Clioquinol	1 (1.1)	4 (0.8)
Colophony	3 (3.2)	23 (4.5)
2,6-Di- <i>tert</i> -butyl-4-cresol	2 (2.2)	8 (1.6)
Formaldehyde	6 (6.5)	29 (5.7)
FM	18 (19.4)	53 (10.5)*
Hexahydro-1,3,5-tris-(2-hydroxyethyl)triazine	5 (5.4)	27 (5.3)
2-Hydroxy-4-methoxybenzophenone	2 (2.2)	5 (1.0)
Imidazolidinyl urea	3 (3.2)	5 (1.0)
Isopropyl myristate	2 (2.2)	6 (1.2)
Octyl gallate	11 (11.8)	65 (12.8)
Paraben mix	5 (5.4)	24 (4.7)
PPD	20 (21.5)*	26 (5.1)
Phenyl salicylate	4 (4.3)	9 (1.8)
Polyoxyethylenesorbitanmonooleate	3 (3.2)	22 (4.3)
Propylene glycol	2 (2.2)	1 (0.2)
Sesquiterpene lactone mix	1 (1.1)	8 (1.6)
Sorbic acid	0	4 (0.8)
Sorbitan monooleate	11 (11.8)	36 (7.1)
2- <i>tert</i> -Butyl-4-methoxyphenol	1 (1.1)	8 (1.6)
Thimerosal	10 (10.8)	70 (13.8)
Triclosan	0	4 (0.8)
Triethanolamine	1 (1.1)	24 (4.7)

CACD, cosmetic allergic contact dermatitis; FM, fragrance mix; PPD, *para*-phenylenediamine.

* $P < 0.05$, patients with CACD versus other patients, chi-squared test.

The PT in patients with suspected CACD showed that PPD and FM were the 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) (2) to 79% in 29 cosmetic-related dermatitis (2000, UK) (12). The most common allergen reported in 50 patients with suspected CACD in India in 2000 was fragrance also (47%) (1). Compared with these reports, FM sensitivity was relatively lower in our case. This difference may be because of the less frequent use of perfumes, deodorants, and other aroma products in China. PPD allergy have been found in 23.5% among 50 patients with suspected CACD (2000, India) (1) and in 23% of 53 suspected allergic contact eczema/dermatitis from cosmetic usage (2002, Spain) (2). Our results are consistent with these results. 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). However, in Spain, PPD contact allergy in hairdressers was found increased from 45.9% to 54% during a 10-year period (1994–2003) (13).

Compared with patients without cosmetic reactions ever, patients with suspected CACD showed higher positivity rates to PPD, FM, Amerchol L 101 and abitol (Table 4). These results indicated that CACD should be strongly considered in CEPs with positive PT reactions to PPD, FM, Amerchol L 101 and abitol.

No significant differences were found in the positivity rates to the other CCA between patients with or without CACD (Table 4). These results indicate that positive PT reactions to these allergens were not mainly cosmetic related in CEPs. Because Chinese regulations do not require cosmetic manufactures labeling their products in China, we cannot confirm the relevance of these positive PT results directly.

We know that although CACD is common, the sensitizing allergens vary between countries and study period (14). Our data only represent a medical center in Beijing; more work should be performed to investigate the CCAs in China.

In summary, our results confirmed that CACD is very common in China. The most common cosmetics causing CACD are skin care products and color decorating products. The leading cosmetic allergens of CACD in CEPs are PPD and FM. Many CCAs yield positive PT reactions in CEPs with positive PT reactions to PPD, FM, Amerchol L 101 and abitol. PT with cosmetic series of allergens is very valuable in screening CACD in CEPs. Strict regulation is definitely needed in China to ensure that the cosmetic manufactures labeling their products.

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Address:

Dr Lin-Feng Li
Department of Dermatology
Peking University Third Hospital
49 North Garden Road
Haidian District
Beijing 100083
China
Tel: +86 1062017691x2660
Fax: +86 1062017700
e-mail: zoonli@tom.com