

A study of the sensitization rate to cocamidopropyl betaine in patients patch tested in a university hospital of Beijing

LIN-FENG LI

Department of Dermatology, Peking University Third Hospital, 49 North Garden Road,
Haidian District, Beijing 100083, China

Background: The prevalence of sensitization to cocamidopropyl betaine (CAPB) in China has not been reported.

Objective: This study is to evaluate the prevalence of CAPB sensitization in patients patch tested in Peking University Third Hospital, Beijing.

Methods: 429 consecutive patients with suspected allergic contact dermatitis were patch tested with CAPB 1.0% aqueous, 3-dimethylaminopropylamine (DMAPA) 1.0% aqueous as well as a modified European standard series of allergens from June 2005 to August 2006.

Results: 42 patients (9.8%) had a positive reaction to CAPB. 25 of them (59.5%) were considered relevant. Of those, 7 were head and/or neck dermatitis, 4 hand dermatitis, 1 cheilitis, and the other 13 patients were widespread dermatitis. 10 out of 429 (2.3%) patients reacted to DMAPA. Of those, 8 were relevant and 6 of them also reacted to CAPB.

Conclusion: The rate of CAPB sensitization in our study is higher than previously reported elsewhere. CAPB is a common cosmetic allergen in Beijing. Both CAPB and DMAPA should be tested in patients with suspected cosmetic dermatitis.

Key words: allergy; CAPB; cocamidopropyl betaine; contact dermatitis; cosmetics; dimethylaminopropylamine; DMAPA; patch test; prevalence; surfactant. © Blackwell Munksgaard, 2007.

Accepted for publication 14 July 2007

Cocamidopropyl betaine (CAPB) is an amphoteric surfactant commonly used in rinse-off personal care products including liquid soaps, shampoos, hair colourants, shower, and bath formulations. It has been identified as a common cosmetic allergen for more than 20 years (1–8). The reported prevalence of CAPB allergy worldwide ranged from 1.4% to 7.2% depending on the population studied (Table 1) (1–7). Recent studies have suggested that residues present in some commercial grades of the surfactant, such as amidamine, 3-dimethylaminopropylamine (DMAPA) may be the true allergens of CAPB allergy, and allergy can be avoided if aminopropylamines have been removed (2, 9). Recent studies from the USA, Australia, and Israel, however, suggest that CAPB allergy remains a clinical problem, and

CAPB should be included in routine patch tests (1–3, 10). China is a big cosmetic consumer in the world where CAPB is widely used (11, 12); the prevalence of allergy to CAPB in China has not been reported. The purpose of this study was to: (i) determine the sensitization rate to CAPB in patients patch tested in a university hospital in Beijing by using CAPB (Tegobetaine F50) patch testing and (ii) analyse the relationship between CAPB and DMAPA patch testing.

Patients and Methods

Study population

429 patients with suspected contact allergy referred by other dermatologists were patch tested in Peking University Third Hospital between June

Table 1. Reported prevalence of cocamidopropyl betaine allergy

References	Patients studied	Prevalence (%)	Relevance (%)
Raz et al. (1)	100 suspected CACD patients	6	66
Brey et al. (2)	957 ACD patients	2.2	82.9
Fowler et al. (3)	975 suspected ACD patients	3.4	48
De Groot et al. (4)	781 dermatitis patients	7.2	30.4
Pigatto et al. (5)	1190 unselected eczema	1.4	Not reported
Angelini et al. (6)	1200 unselected dermatitis	3.8	100
Fowler (7)	210 suspected CACD and/or head and neck dermatitis	5.7	58.3

ACD, allergic contact dermatitis; CACD, cosmetic allergic contact dermatitis.

2005 and August 2006. There were 105 men and 324 women with age range from 9 to 81 years. All patients were Chinese Han ethnics. Local ethics committee approved this study, and the participants gave oral consent.

Patch testing

Patch testing was performed with CAPB 1.0% aqueous and DMAPA 1.0% aqueous (Chemotechnique Diagnostics, Malmö, Sweden). Chemotechnique Diagnostics has provided written confirmation that their CAPB 1.0% aqueous is prepared from Tegobetaine F50 in which aminopropylamines have been removed. European standard series of allergens (Chemotechnique Diagnostics) were tested simultaneously using improved quality chamber (Chemotechnique Diagnostics). Allergens were applied to the upper back and removed after 2 days. The results were recorded at 2 days and 3 days according to International Contact Dermatitis Research Group grading (13). After testing, the suspected causal agent was investigated using a questionnaire (14), in which, patient's personal data, present illness, contactant existed in work, clothes, toiletries, household and treatment, atopic diathesis as well as medications taking presently or within last 3 months were included. Clinical relevance of patch testing was defined as present if the patient had a cosmetic allergic contact dermatitis (CACD) to a rinse-off product, which may contain CAPB. Because cosmetic ingredient labelling is not mandatory in China, definite relevance of CAPB patch testing could not be analysed directly so far. Relevance was graded as 'probable' if there were no other significant positive patch test reactions and if the

dermatitis definitely improved with avoidance of the product; 'possible' other significant allergens were present; and 'not relevant' if there was no relation between the dermatitis and the usage of cosmetics (2, 3).

Diagnostic criteria

CACD was suspected by the following criteria: (i) Cosmetics had been used before the development of dermatitis and (ii) Dermatitis had been definitely improved after the discontinuation of the suspected cosmetics. If a patient with suspected CACD could reapply the suspected cosmetics without any reactions, CACD was excluded. If CACD was elicited more than twice by the same cosmetics, CACD was confirmed.

Statistic analysis

The data were processed by chi-squared test and Rank Sum test with statistic software spss 11.0.

Results

Of 429 patients tested, 9 irritant reactions, 12 questionable reactions, and 42 + positive reactions to CAPB were recorded. No reactions greater than ++ were found. The total positivity rate to CAPB was 9.8% (42/429). CACD were diagnosed in 76 patients. 27 out of 76 CACD patients (35.5%) and 15 out of 353 non-CACD patients (4.2%) had a positive reaction to CAPB ($P < 0.05$, chi-squared test). In 27 CACD patients reacted to CAPB, 25 cases were considered relevant (Table 2), of those non-CACD patients, none was relevant. 10 out of 429 (2.3%) patients had a positive reaction to DMAPA. Of those, 8 were relevant, and 6 of them also reacted to CAPB.

Table 2 showed the clinical features of CAPB test positive CACD patients. A comparison between CACD patients with or without CAPB allergy is given in Table 3.

Discussion

In Europe, it has been considered that CAPB allergy was largely because of the presence of amidopropylamines in Tegobetaine L7 (Goldschmidt, Essen, Germany); when L7 was replaced with Tegobetaine F50 (Goldschmidt), in which aminopropylamines have been removed; CAPB contact allergy was no longer a clinical problem. However, recent studies from the USA, Australia, and Israel indicate that CAPB allergy remains of a clinical concern in these geographical

Table 2. Clinical features of CAPB patch test positive CACD patients

Number	Age (years)/sex	Location of CACD	Causative cosmetics	Relevance ^a	Concomitant positive patch test
1	36/F	Face	Facial cream	Not relevant	Parabens, nickel, and DMAPA
2	32/F	Face	Face cleanser	Possible	Nickel and Formaldehyde
3	32/F	Face	Face cleanser	Probable	None
4	35/F	Face	Facial cream	Not relevant	Thimerosal (merthiolate)
5	39/F	Face	Face cleanser	Probable	None
6	35/F	Face	Face cleanser	Probable	Nickel
7	60/M	Face	Shampoo	Possible	Imidazolidinyl urea
8	32/M	Face and neck	Hair dye	Possible	PPD, nickel, and carba mix
9	22/F	Face, neck, and hand	Liquid soap	Probable	None
10	20/F	Cheilitis	Toothpaste	Possible	Thimerosal (merthiolate)
11	19/M	Widespread	Shampoo	Possible	DMAPA, formaldehyde, <i>N</i> -(cyclohexylthio) phthalimide, and thimerosal (merthiolate)
12	58/M	Widespread	Shampoo	Probable	Carba mix and DMAPA
13	39/M	Widespread	Shampoo	Possible	DMAPA, formaldehyde, 2-bromo-2-nitropropane-1,3-diol (bronopol), and carba mix
14	37/F	Widespread	Shampoo	Possible	Parabens, fragrance mix, carba mix, and black rubber mix
15	57/F	Widespread	Hair dye	Possible	PPD
16	67/M	Widespread	Both gel	Possible	Colophonium
17	30/F	Widespread	Both gel	Probable	None
18	50/M	Widespread	Both gel	Probable	<i>N</i> -(cyclohexylthio) phthalimide
19	35/F	Widespread	Both gel	Probable	Nickel
20	78/M	Widespread	Hair dye	Probable	DMAPA
21	50/F	Widespread	Hair dye	Probable	DMAPA
22	42/M	Widespread	Both gel	Possible	Formaldehyde, DMAPA
23	43/F	Widespread	Both gel	Probable	None
24	41/F	Hand	Liquid soap	Probable	Nickel
25	62/F	Hand	Liquid soap	Probable	None
26	47/F	Hand and neck	Liquid soap	Probable	None
27	33/M	Hand and neck	Liquid soap	Probable	None

ACD, allergic contact dermatitis; CACD, cosmetic allergic contact dermatitis; CAPB, cocamidopropyl betaine; DMAPA, 3-dimethylaminopropylamine; F, female; M, male; PPD, 4-phenylenediamine base.

^aBecause ingredients labelling is not mandatory in China, relevance cannot be analysed directly (see Patients and Methods).

areas and routine patch testing with CAPB is recommended (1–3, 10). In this study, we tested patients with 1.0% CAPB prepared from Tegobetaine F50 (Goldschmidt); therefore, our results are CAPB specific. Our data showed a high-positivity rate to CAPB, which is much higher than the rates reported (1–8). Knowing that CAPB is a contact allergen with known irritant potential, we excluded a large number of irritant and doubtful reactions. The sensitization rate (9.8%), however, is still high. We think that most of those were not irritant, because the positivity rate to CAPB patch testing in CACD patients was much higher than that in non-CACD patients (35.5% versus 4.2%), which is strongly supported that the test result was related to CAPB sensitization. The clinical features of CAPB positive CACD in our hands were also in accordance with CAPB allergy reported (Table 2) (1–8); the most frequent site of dermatitis is the head and neck region, hands are also affected, widespread dermatitis attributed to CAPB in shampoo has also been noted.

CAPB is widely used in China. The Chinese literature indicates that some grades of the surfactant do contain amidopropylamines (11, 12). The

structural formula of CAPB is $C_{11\sim 17}H_{23\sim 35}CONH(CH_2)_3N^+(CH_3)_2CH_2COO^-$, the structural formula of amidopropylamines are $H_2N(CH_2)_3N(CH_3)_2$ and $C_{11\sim 17}H_{23\sim 35}CONH(CH_2)_3N(CH_3)_2$

Table 3. Comparisons between CACD patients with and without CAPB sensitization

	CAPB test positive (<i>n</i> = 27)	CAPB test negative (<i>n</i> = 49)
Age (mean ± SD)	41.9 ± 14.2	42.0 ± 15.3
Sex (male:female)	10:17	4:45*
Atopic diathesis	5	6
Occupational dermatitis	0	4 (all hair dressers)
Face and/or neck dermatitis	9	27
Widespread dermatitis	13	8*
Causative rinse-off cosmetics	25	31*
Nickel allergy	7	13
Fragrance mix allergy	1	6
Formaldehyde	4	8
4-phenylenediamine base allergy	2	16*

CACD, cosmetic allergic contact dermatitis; CAPB, cocamidopropyl betaine.

**P* < 0.05, chi-squared test.

(11, 12). As we used Tegobetaine F50 in our patch testing, we do not consider that it is important whether the commercial grades of CAPB used in China contain amidopropylamines or not; the patch test were CAPB specific.

Because ingredients labelling is not mandatory in China, the relevance of CAPB patch testing could not be analysed directly. Of those test positive patients, 15 (55.6%, 15/27) reacted to no other allergens or only to non-cosmetics related allergens besides CAPB suggesting that these patch test results probably relevant. Interestingly, the single positive allergen in 2 patients with widespread dermatitis because of hair dye (number 20 and 21, Table 2) was CAPB strongly supported that it was the causative allergen. These findings suggested that CAPB allergy is very common in China and should be tested in patients with suspected CACD.

There was no significant difference in age, atopic diathesis, face, and/or neck dermatitis between CAPB-positive- and negative-CACD patients. Men were over presented in CAPB positive group, so did the widespread dermatitis (Table 3). Because CAPB is frequent in rinse-off cosmetics, which are used equally by men and women in China, while men use much less stay-on products (Table 3), it is reasonable to find more men in CAPB positive group. Rinse-off products such as shampoo will surely cause more widespread dermatitis than the cosmetics used locally.

Different to the literature (2), no significant difference was found in the positivity rate to nickel, fragrance mix, and formaldehyde between CAPB tested positive- and negative patients (Table 3). The positivity rate to 4-phenylenediamine base was significantly higher in CAPB test negative group. The mechanism of it is unknown. However, more women in this group may contribute partly to it.

The results of DMAPA patch testing clearly showed that the sensitization to DMAPA was also common. 2 CAPB allergic patients only reacted to DMAPA; therefore, both CAPB and DMAPA should be patch tested in patients with suspected CACD.

Acknowledgement

This work was supported in part by a special fund for promotion of education from the Ministry of Educa-

tion, China and national '211 project' Peking University evidence-based medicine group (project no: 93000-246156071) (L-F. Li).

References

1. Raz O, Slodownik D, Ingber A. Allergic contact dermatitis to cocamidopropyl betaine among Israeli patients with cosmetic allergy. *Harefuah* 2006; 145: 486–488, 551.
2. Brey N L, Fowler J F. Relevance of positive patch-test reactions to cocamidopropyl betaine and amidoamine. *Dermatitis* 2004; 15: 7–9.
3. Fowler J F, Zug K M, Taylor J S et al. Allergy to cocamidopropyl betaine and amidoamine in North America. *Dermatitis* 2004; 15: 5–6.
4. de Groot A C, van der Walle H B, Weyland J W. Contact allergy to cocamidopropyl betaine. *Contact Dermatitis* 1995; 33: 419–442.
5. Pigatto P D, Bigardi A S, Cusano F. Contact dermatitis to cocamidopropyl betaine is caused by residual amines: relevance, clinical characteristics, and review of the literature. *Am J Contact Dermat* 1995; 6: 13–16.
6. Angelini G, Foti C, Rigano L, Vena G A. 3-dimethylaminopropylamine: a key substance in contact allergy to cocamidopropyl betaine? *Contact Dermatitis* 1995; 32: 96–99.
7. Fowler J F. Cocamidopropyl betaine: the significance of positive patch test results in 12 patients. *Cutis* 1993; 52: 281–284.
8. Brand R, Delaney T A. Allergic contact dermatitis to cocamidopropylbetaine in hair shampoo. *Australas J Dermatol* 1998; 39: 121–122.
9. Hervella M, Yanguas J I, Iglesias M E, Larrea M, Ros C, Gallego M. Contact allergy to 3-dimethylaminopropylamine and cocamidopropyl betaine. *Actas Dermosifiliogr* 2006; 97: 189–195.
10. Agar N, Freeman S. Cheilitis caused by contact allergy to cocamidopropyl betaine in '2-in-1 toothpaste and mouthwash'. *Australas J Dermatol* 2005; 46: 15–17.
11. Tu H, Man R, Chen W. The development of the multi-purpose amphoteric surfactant of cocamidopropyl betaine. *Deterg Cosmet* 2001; 24: 44–46.
12. Qian CH. Preparation of cocamidopropyl betaine directly from coconut oil. *Fine Spec Chem, Cyclohexythio* 2004; 12: 17–18.
13. Wahlberg J E, Lindberg M. Patch testing. In: *Textbook of Contact Dermatitis*, 4th edition, Frosch P J, Menné T, Lepoittevin J-P (eds): Berlin, Springer, 2006: 365–390.
14. Pellegrini A E. Establishing a contact/occupational dermatitis clinic: practical considerations. *J Assoc Mil Dermatologists* 1985; 9: 8–16.

Address:

Dr Lin-feng Li
Department of Dermatology
Peking University Third Hospital
49 North Garden Road
Haidian District
Beijing 100083
China
Tel: 011861062017691ext2660
Fax: 011861062017700
e-mail: zoonli@sina.com