

Short communication

Contact urticaria from protein hydrolysates in hair conditioners

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Protein hydrolysates (PHs) are added to hair-care products (to “repair” broken hair), soaps, bath gels, creams, etc. From one to 22 PHs used in hair-care products (collagen, keratin, elastin, milk, wheat, almond, and silk) were tested in three patient groups:

- A) 11 hairdressers with hand dermatitis
- B) 2160 consecutive adults with suspected allergic respiratory disease subjected to routine skin prick tests
- C) 28 adults with atopic dermatitis.

In group A, all the 22 PHs were tested with scratch and patch tests. In groups B and C, one to three PHs were tested with prick tests. Positive scratch/prick test reactions were seen in 12 patients from three PHs altogether. All were women with atopic dermatitis, and all reacted to at least hydroxypropyl trimonium hydrolyzed collagen (Crotein Q®). In three patients, prick and open tests with a hair conditioner containing Crotein Q were performed with positive results. One patient reported contact urticaria on her hands, and two reported acute urticaria on their head, face, and upper body from a hair conditioner containing Crotein Q. In seven of the eight studied sera, specific IgE to Crotein Q was detected. In conclusion, PHs of hair cosmetics can cause contact urticaria, especially in patients with atopic dermatitis.

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Protein hydrolysates (PHs) are added to hair conditioners to “repair” broken hair and to give the hair a more voluminous appearance. They are also added to other hairdressing products and skin-care products, such as soaps, bath gels, creams, etc. PHs in hair conditioners have occasionally been reported to cause immediate urticarial skin reactions, even angioedema and bronchospasm (1–3). One of the two patients reported by Kousa et al. (1) was examined in the department of dermatology of the University Hospital of Oulu, Finland. She was a hairdresser with contact urticaria on her hands caused by a PH in a hair conditioner. She also began to get contact urticaria from other hair-care products. Therefore, we tested her and 10 other hairdressers, 2160 adult patients with suspected allergic respiratory disease subjected to routine skin prick testing, and 28 adults with atopic dermatitis with a larger assortment of PHs. The

results suggest that PHs might cause immediate skin reactions more frequently than previously recognized, especially in patients with atopic eczema.

Material and methods

Patients

Three patient groups were studied. Group A comprised 11 hairdressers examined for hand dermatitis. Group B comprised 2160 consecutive adults (>15 years) referred for prick tests because of suspected IgE-mediated respiratory symptoms. These patients came from the departments of otorhinolaryngology and internal medicine of Oulu University Hospital or from private offices or health-care centers of the Oulu region. Group C comprised 28 adults with chronic atopic dermatitis.

Table 1. Twenty-two protein hydrolysates, all of which were tested in 11 patients (group A), three (nos. 6, 10, and 17) in 1260 patients (1232 in group B and all 28 in group C), and one (no. 6) in 928 patients of group B. Product names italicized are products of Henkel; others of Croda

Trademark	INCI (International Nomenclature Cosmetic Ingredient) name
Collagen	
1. Collasol	Soluble collagen
2. Cropepsol 50	Hydrolyzed collagen ^{a1}
3. Croquat L	Lauryldimonium hydroxypropyl hydrolyzed collagen
4. Crotein A	Hydrolyzed collagen ^{a1}
5. Crotein C	Hydrolyzed collagen
6. Crotein Q	Hydroxypropyl trimonium hydrolyzed collagen ^{b1}
7. <i>Lamepon ST 40</i>	<i>TEA-cocoyl hydrolyzed collagen^{c1}</i>
8. <i>Lamepon STR</i>	<i>TEA-cocoyl hydrolyzed collagen^{c1}</i>
9. <i>Lamequat L</i>	<i>Lauryldimonium hydroxypropyl hydrolyzed collagen</i>
10. <i>Nutrilan H</i>	<i>Hydrolyzed collagen^{a1}</i>
11. <i>Nutrilan I powder</i>	<i>Hydrolyzed collagen^{a1}</i>
Elastin and keratin	
12. Crolastin 30	Hydrolyzed elastin
13. <i>Nutrilan Elastin P</i>	<i>Hydrolyzed elastin</i>
14. Croquat WKP	Cocodimonium hydroxypropyl hydrolyzed keratin
15. Crotein HKP S/F	Keratin amino acids
16. <i>Nutrilan Keratin W</i>	<i>Hydrolyzed keratin</i>
Milk, wheat, almond, and silk	
17. Hydrolactin 2500	Hydrolyzed milk protein
18. Hydrolactin Quaternised Powder	Hydroxypropyl trimonium hydrolyzed milk protein ^{a1}
19. Crodasone W	Hydrolyzed wheat protein hydroxypropyl siloxane
20. <i>Gluadin AGP</i>	<i>Hydrolyzed wheat protein</i>
21. Hydromond	Hydrolyzed sweet almond protein
22. Cosilkquat 10.000	Cocodimonium hydroxypropyl hydrolyzed silk

^{a1} Differ from Crotein C only in having lower average molecular weights.

^{b1} Other generic name: stearyltrimonium hydroxyethyl hydrolyzed collagen.

^{c1} Same product with different solid contents.

^{d1} Different forms of same collagen: "H" is liquid, "I" is powder.

^{e1} Still under development, not in commercial use. There is no agreed INCI name.

Skin tests

Twenty-two PHs (Table 1) obtained from two Finnish companies producing shampoos and other hairdressing products were tested with scratch or prick tests (1% in saline) and with patch tests (5% in saline). In the patients of group A, all the 22 PHs were tested with both scratch and patch tests. In the patients of groups B and C, only prick tests were performed as follows: three PHs (nos. 6, 10, and 17 in Table 1) were tested in 1232 patients of group B and in all patients of group C, while only one PH (Crotein Q[®], no. 6 in Table 1) was tested in 928 patients of group B. Prick tests with undiluted and 1:10 and 1:100 aqueous solutions of a commercial hair conditioner containing Crotein Q were performed on three patients with a positive prick test to Crotein Q. All patients were also tested with a standard prick test series including two house-dust

mites, animal epithelia (horse, cow, cat, and dog), tree pollens (birch and alder), four grass pollens, and mugwort pollen (Soluprick[®]; ALK, Hørsholm, Denmark), as well as with a natural rubber latex solution prepared according to the recommendations of Turjanmaa (4). In group A, prick tests with milk, wheat, and almond (Soluprick) were also performed.

In the scratch and prick tests, the recommendations of the Subcommittee on Skin Tests of the European Academy of Allergology and Clinical Immunology (5) were followed. The tests were considered positive if a reaction at least 50% as large as that produced by 1% histamine dihydrochloride and at least 3 mm in diameter (transverse axis in the scratch tests) was noticed.

Open tests with an undiluted commercial hair conditioner containing Crotein Q were performed on three patients with positive prick tests to Crotein Q and with positive prick tests to that particular hair conditioner. In two of them, tests were also performed with 1:10 and 1:100 aqueous solutions of the conditioner. Open tests were made by spreading the test material on a 5 × 5 cm area of the healthy, volar side of a forearm. The area was followed up for 60 min. The tests were considered positive if urticarial lesions appeared on the test area.

In patch tests, 5% test solutions were put on a filter paper in Finn Chambers[®] on Scanpor[®] (Epitest Ltd, Tuusula, Finland) and fixed on the back skin for 2 days. The patch tests were read on day 2, 30–60 min after removing the patches. If the day 2 result was negative, the patient was asked to monitor the tests at home and to contact the clinic if any reaction appeared. The patch test was considered positive if a reaction with erythema and infiltration was noticed.

Specific IgE determinations

In group A, specific serum IgE to two PHs (Crotein Q and Hydrolactin Quaternised Powder[®]) was determined with the radioimmunoassay method (RAST) of Pharmacia (Uppsala, Sweden). In groups B and C, specific serum IgE to Crotein Q was studied by one of us (S.M.-K.) as follows: 10 mg of Crotein Q powder was dissolved in 1 ml of sodium bicarbonate (100 mM). A volume of 100 µl of the solution was coupled to cyanogen bromide-activated paper disks (6). The results were calculated from a standard birch IgE curve supplied with the Phadebas RAST kit and expressed as PRU/ml. Specific IgE values higher than 0.35 PRU/ml were regarded as positive.

Sera from eleven patients (seven women, four men, aged 16–49 [mean 30] years) with negative prick tests to Crotein Q were used as controls.

Table 2. Positive skin prick/scratch test results with protein hydrolysates (PHs) used in hair conditioners. Crotein Q was tested on all 2199 patients. In addition, 21 PHs (Table 1) were tested on all patients of group A, and Nutrilan H and Hydrolactin 2500 on 1232 patients of group B and all patients of group C. PHs were tested with scratch tests in group A and with prick tests in groups B and C

Patient no.	Sex/age (years)	Current dermatitis, if any	Skin prick/scratch tests with Crotein Q (%)				Positive prick/scratch test reactions to other PHs	Patients' observations on symptoms from hair conditioner
			1	.1	.01	.001		
Group A; 11 hairdressers with hand dermatitis								
1.	F/37	Hands	+	+	+	+	Hydrolactin Quaternised Powder (1–0.001%)	Contact urticaria
Group B; 2160 consecutive adults subjected to skin prick tests for suspected allergic respiratory symptoms								
2.	F/22	Eyelids, neck, hands, arms, legs	+	+	+	+	None	None
3.	F/22	Hands	+	+	+	–	None	None
4.	F/26	Face, hands, scalp	+	+	+	+	None	None
5.	F/29	Neck, legs	+	+	+	+	None	None
6.	F/27	Generalized, face and hands included	+	+	+	+	None	None
7.	F/16	Face, neck, arms, thighs	+	+	+	+	None	Conjunctivitis
8.	F/25	Hands, face occasionally	+	+	+	+	None	None
9.	F/34	Rhinitis only ^{a)}	+	+	+	+	None	None
10.	F/25	Asthma only	+	ND ^{b)}	ND	ND	Nutrilan H (1%)	None
Group C; 28 adults with chronic atopic dermatitis								
11.	F/28	Hands, neck, arms, legs	+	+	+	+	Nutrilan H (1%)	Contact urticaria
12.	F/33	Face, hands, neck, upper body	+	+	+	+	Nutrilan H (1%)	Contact urticaria

^{a)} Previously dermatitis on face, neck, and hands.

^{b)} Not done.

These 11 patients had been referred for prick tests for their respiratory symptoms, and all had positive SPT reactions to one or more allergens in the standard SPT series (nine to animal epithelia, seven to grass pollens, five to tree pollens (birch or alder), two to mugwort pollen, and one to house-dust mite (*Dermatophagoides pteronyssinus*). In addition, a pool of 20 sera from nonatopic persons and another pool of 15 sera from atopic patients (bee-venom allergics) were used as controls.

Results

The positive skin test results from PHs are summarized in Table 2. All the 12 patients with a positive scratch or prick test reaction to any of the PHs reacted to hydroxypropyl trimonium hydrolyzed collagen (Crotein Q). One patient also reacted to quaternized hydrolyzed milk protein (Hydrolactin Quaternised Powder), and three to hydrolyzed collagen (Nutrilan H[®]). Crotein Q and Hydrolactin Quaternised Powder elicited clear-cut, usually large reactions: 4–20 (mean 11) mm in diameter. In end-point titrations, both Crotein Q and Hydrolactin Quaternised Powder elicited positive reactions in very low concentrations (Table 2, Fig. 1). On the contrary, all the prick

test reactions to 1% Nutrilan H were small (3 mm in diameter). In one case, tests with lower concentrations (1:10 and 1:100) of Nutrilan H were also performed with negative results. Patch tests with PHs were negative in all the 11 hairdressers tested (group A).

In all the three patients tested (nos. 6, 11, and 12 in Table 2), the prick and open tests to both undiluted and diluted hair conditioner containing Crotein Q were positive. The open tests appeared as erythema with a few small wheals (3–4 mm in diameter) on the test area within 30 min.

Eleven of the 12 patients with positive reactions to PHs had positive reactions to one or more allergens of the standard prick test series. Eight reacted to animal epithelia (all to dog, seven to cat, six to horse, and one to cow), six reacted to grass pollens, three to tree pollens, one to mugwort pollen, one to house-dust mite, and one to natural rubber latex. In group A, almond elicited a positive reaction in one patient (no. 1 in Table 2), while milk and wheat elicited no positive reactions.

Specific IgE to Crotein Q was determined in the sera of eight patients, in 11 individual control sera, and in two serum pools. In seven patients, elevated values (0.4–1.2 PRU/ml, mean 0.7 PRU/ml) were observed. All the controls remained negative.

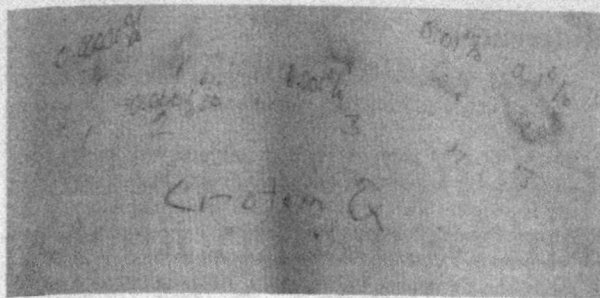


Fig. 1. Positive prick test reactions in end-point titration with hydroxypropyl trimonium hydrolyzed collagen (stearyltrimonium hydroxyethyl hydrolyzed collagen; Crotein Q) in patient with atopic dermatitis (no. 4 in Table 2).

Specific serum IgE to Hydrolactin Quaternised Powder was determined in one patient of group A (no. 1 in Table 2) and was found to be elevated with a value of 0.7 PRU/ml. No determination of specific IgE to Nutrilan H was performed.

All the 12 patients with positive scratch or prick test reactions to PHs were female atopsics (Table 2). Ten of them had active atopic dermatitis, mostly on the hands and the face. One (no. 9 in Table 2) had previously had dermatitis with a similar distribution. Four patients reported symptoms from hair-washing products. The hairdresser (no. 1 in Table 2) had noticed itching and urticaria on her hands, sometimes itching even from her customers' dry hair. Two patients (nos. 11 and 12 in Table 2) had had urticaria on their scalp and face with redness or urticaria on their upper body after using a hair conditioner at home. Both were able to name the offending hair conditioner. One patient (no. 7 in Table 2) reported an episode of conjunctivitis after washing her hair. All these patients had changed their hair-care products after these experiences.

Discussion

In this study, 12 out of 2199 (0.5%) patients showed positive prick or scratch tests to PHs used in hairdressing products. All of them reacted to one particular PH, hydroxypropyl trimonium hydrolyzed collagen (stearyltrimonium hydroxyethyl hydrolyzed collagen; Crotein Q). Two of the 12 patients reported an episode of acute urticarial skin symptoms after hair washing, one reported conjunctivitis, and one (a hairdresser) reported professional contact urticaria on the hands. Three of the four previously reported patients (1-3) have had even more severe symptoms, such as angioedema, general urticaria, and even bronchospasm from using hair conditioners.

Of the 12 patients with positive scratch/prick tests to PHs, 10 had current atopic dermatitis,

mostly on the hands and the face. It is remarkable that seven of the nine patients found among the patients of group B (i.e., patients referred for routine prick tests because of respiratory symptoms) also had atopic dermatitis. Most of the 2160 patients of group B had only respiratory symptoms. The results suggest that PHs in hair conditioners can cause immediate skin responses, especially in subjects with atopic eczema.

The question of whether the positive scratch/prick test reactions to PHs were IgE-mediated or not remained slightly open. The positive prick test reactions to very low concentrations of Crotein Q and Hydrolactin Quaternised Powder suggest that the reactions were IgE-mediated. Furthermore, specific IgE to Crotein Q was found in seven out of eight studied sera and specific IgE to Hydrolactin Quaternised Powder in one studied serum. The levels were relatively low, but completely negative in all control sera. The fact that eight of the 12 patients with positive scratch/prick test reactions to PHs had never noticed any symptoms does not exclude an IgE-mediated mechanism. It is not easy for patients with continually itching eczematous skin to notice aggravation from a particular technicochemical product. The situation could be analogous to the patients with chronic atopic hand dermatitis and IgE-mediated allergy to natural rubber latex. These patients may not notice any symptoms from household rubber gloves used by themselves, although they may develop even serious anaphylactic symptoms from the rubber gloves of an operating surgeon (4).

Hydroxypropyl trimonium hydrolyzed collagen (stearyltrimonium hydroxyethyl hydrolyzed collagen; Crotein Q) seemed to be an especially potent cause of immediate skin reactions in this study. We do not know whether or not some other PHs would have been equally potent, because only Crotein Q was tested in all the 2199 patients. All the 22 PHs were tested in only 11 patients (group A). Apart from Crotein Q, the two other PHs tested in groups B and C, i.e., Hydrolactin 2500 and Nutrilan H, were selected quite randomly. Because Crotein Q and Hydrolactin Quaternised Powder produced big scratch test reactions in one hairdresser (group A), our intention was to use these two PHs also in the prick tests in groups B and C. Hydrolactin Quaternised Powder, however, was no longer available. Therefore, we selected another milk hydrolysate, Hydrolactin 2500[®]. Nutrilan H was included for a comparison between two different collagen hydrolysates (Crotein Q and Nutrilan H).

The feature common to the two PHs, Crotein Q and Hydrolactin Quaternised Powder, which produced the most intense reactions in this study is the

quat group attached to the protein, i.e., hydroxypropyl trimethyl ammonium chloride. In contrast, the other quaternized protein derivatives tested in group A are longer-chain quats (R. T. Jones, Research & Development, Croda Colloids Ltd; personal communication). Whether or not especially hydroxypropyl trimethyl ammonium chloride makes a protein hydrolysate more able to cause immediate skin responses deserves further studies.

In conclusion, PHs used in hair conditioners, especially Crotein Q, may cause immediate skin reactions manifested as contact urticaria, especially in subjects with atopic eczema. The symptoms can be assessed with prick tests with the suspected PHs. The tests can also be performed with the suspected hair conditioner as such, if the particular PHs are not available.

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