

Specific immunoglobulin E in patients with immediate persulfate hypersensitivity

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Persulfate salts may cause contact urticaria, allergic and irritant contact dermatitis, rhinitis and asthma. The mechanism of the immediate reactions has been unclear. Positive prick test, skin application and nasal and bronchial provocations identify immediate allergy. There is only 1 previous report of specific binding of immunoglobulin E (IgE) to ammonium persulfate demonstrated by radioallergosorbent test (RAST). In the present study, fresh 2% ammonium and potassium persulfate solutions were used for prick testing. Patients with positive prick tests were further evaluated with open skin application, immunospot and RAST. Prick testing with persulfate salts was performed in a total of 138 patients. 7 patients had a positive reaction to at least 1 persulfate salt. 6 of the patients had had skin symptoms, urticaria, eczema or angioedema, because of contact with hair bleaches. Open application on healthy skin was performed in 4 patients, and 3 out of them had urticarial reactions. The sera of 5 patients were investigated with immunospot and RAST. On immunospot, specific binding of IgE to human serum albumin (HSA)-conjugated ammonium and potassium persulfate was found in 2 patients. 1 immunospot-positive patient also had a positive RAST to ammonium persulfate–HSA conjugate. The mechanism of immediate hypersensitivity to persulfates thus seems to be IgE-mediated at least in some patients.

Key words: contact urticaria; immunospot; persulfates; RAST; specific IgE. © Blackwell Munksgaard, 2003.

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Persulfate salts are widely used in hair-bleaching formulas. They have a strong oxidizing action that accelerates the bleaching process and also makes the hair more receptive to the dyes, especially the light shades (1). These chemicals are also used in the chemical (1), pharmaceutical and textile industries as well as in photography and food preservation (2). Consumers may have contact with persulfates in hair bleaches and dental prosthesis cleansers (3).

In 1963, persulfate salts were reported to cause local urticarial reactions on skin contact (4). Since then, there have been several reports of adverse effects, including irritant (2) and allergic contact dermatitis (1), local and generalized urticaria (1, 5), rhinitis (1, 6), asthma (1, 7, 8) and even vascular collapse (5).

The mechanism of the immediate reactions is unclear. Positive prick tests (7), scratch (1) and intradermal (4) tests, skin application (1, 5) and nasal (6) and bronchial (7, 8) provocations identify immunoglobulin E (IgE)-mediated allergy, but passive transfer tests have been negative (4).

There is only 1 previous report of a positive radioallergosorbent test (RAST) to ammonium persulfate in a patient with contact urticaria, rhinitis and asthma (9). Other attempts to demonstrate specific Igs have failed (7, 10).

For such skin tests, the importance of using freshly prepared solutions has been emphasized (11). A concentration of 2% has been recommended for prick testing (11). Many investigators have used higher concentrations (7, 10, 12). Prick tests in control patients have been negative (7, 10, 12). Saturated (4, 5) or 5% (1) solutions of persulfate salts have provoked urticarial reactions in open skin application. Open application tests in control patients have been negative (1, 5). Patch tests with ammonium persulfate (1–2.5%) have produced urticarial reactions (9, 13) and an anaphylactoid reaction (13).

We wanted to study the relevance of positive persulfate prick tests with open skin application and to try to demonstrate specific binding of IgE with RAST and immunospot techniques in patients with positive prick tests to persulfate.

Materials and Methods

Patients with a suspicion of allergic symptoms from contact with hair cosmetics were prick tested with persulfate salts in our hair cosmetic series.

For prick testing, 2% solutions were prepared by adding 0.7 ml sterile water to 14 mg ammonium (Sigma A-6761, Sigma Chemicals, St Louis, MO, USA) and potassium (BDH Laboratory Supplies, Poole, UK) persulfate salts. The skin test was performed within 30 min. The prick test was regarded as positive when the wheal size was at least 3 mm.

For the open application test, 5% solutions were prepared by adding 0.8 ml sterile water to 42 mg of ammonium and potassium persulfate salts. The fresh 5% solution was applied to healthy forearm skin and gently rubbed into the skin. Sterile water was used as negative control.

Prick testing and open application were performed in 20 control patients who had no suspicion of symptoms from hair cosmetics.

2-day patch tests were performed, using Finn Chambers[®] (Epitest Oy, Tuusula, Finland) and Scanpor[®] tape (Norgesplaster A/S, Vennesla, Norway), when allergic contact dermatitis was suspected. Readings were made on D2 and D4 day according to ICDRG recommendations.

In-house immunospot and RAST methods were used to detect specific binding of IgE antibodies to persulfates and their albumin conjugates in 5 sera (14). For the tests, impregnated stock solutions were made from ammonium persulfate (1 g/ml) (Sigma Chemicals) and potassium persulfate (0.5 g/ml) (BDH Laboratory Supplies), in both 0.1 mol/l potassium phosphate buffer, pH 7.2 and 3% human serum albumin (HSA, A-1653, Sigma Chemicals) solution in 9% sodium bicarbonate to gain haptenization as HSA conjugates. Solutions were carefully heated to increase solubility. For the immunospot analysis, 3 µl in duplicates of the clear supernatant and 3 sequential fivefold dilutions thereof were applied to a nitrocellulose sheet (Trans-blot transfer medium, BIO-RAD, Hercules, CA, USA). Pure HSA (3%)

(1/1, 1/5, 1/25 v/v) and a birch pollen skin test preparation (Soluprick[®], ALK, Horsholm, Denmark) in duplicates were used as control antigens. IgE binding was detected by radiolabelled anti-IgE (Pharmacia, Uppsala, Sweden) on autoradiography (14).

For the RAST assay, frozen-stored persulfate-HSA stock solutions were used to gain solid-phase allergens on activated paper discs according to the manufacturer (Immobilon Affinity membranes, Millipore, Billerica, Mass., USA). For a disc, 100 µl of ammonium or potassium persulfate conjugate in 1/3 v/v dilution in 0.1 mol/l potassium phosphate buffer, pH 7.4, was used as coating allergen in an overnight incubation at room temperature. Free binding sites were blocked by incubation for 2 h with 8% monoethanolamine in 1 mol/l sodium bicarbonate, pH 9.5. Finally, discs were washed with 0.1 mol/l potassium phosphate buffer, pH 7.4, containing 3 mmol/l sodium azide and 0.5% Tween 20. For both assays, serum from a nonatopic subject and a serum pool from pollen-allergic atopics were used as control sera. Standards from Pharmacia RAST kit were used for quantifications. Values higher than 0.35 Pharmacia RAST Unit/ml (PRU/ml) were considered positive.

Results

During 1995–98, prick tests with ammonium and potassium persulfate salts were performed in a total of 138 patients. 7 patients (5%), all of them hairdressers, had positive reactions to at least 1 persulfate salt (Table 1). In addition, 1 hairdresser's client with angioedema and dyspnoea during hair bleaching had 5 mm reactions to both persulfate salts, but because of mild dermographism (negative control 2 mm) the test was considered unreliable. 20 control patients were negative on prick testing with 2% ammonium and potassium persulfate salts.

6 hairdressers with positive prick tests had had skin symptoms, urticaria, angioedema or eczema

Table 1. Results of prick tests, open application, immunospot, radioallergosorbent test (RAST) and patch tests

Patient number	Age (years) (sex)	Prick test (mm) (K/NH ₄ -PS)	Open application (K/NH ₄ -PS)	Immunospot (K/NH ₄ -PS-HSA)	RAST (K/NH ₄ -PS-HSA)	Patch test (NH ₄ -PS)
1	22 (F)	0/4	-/+	NS/NS	-/-	-
2	25 (M)	5/3	-/-	NS/NS	-/-	ND
3	22 (F)	4/5	+/+	+/+	-/-	?+
4	45 (M)	0/4	+/+	+/+	-/+	++
5	40 (F)	4/2	ND	NS/NS	-/-	-
6	29 (F)	7/3	ND	ND	ND	++
7	29 (F)	0/4	ND	ND	ND	-

F = female; HSA = human serum albumin; M = male; ND = not done; NS = non-specific; PS = persulfate.

from contact with hair bleaches. 4 out of them also had rhinitis and 2 out of them also had conjunctivitis. 1 hairdresser had had only respiratory symptoms, rhinitis and dyspnoea aggravated at work. 3 of the patients stopped working as hairdressers, 2 because of respiratory symptoms and 1 because of skin symptoms, angioedema and contact urticaria. Immediate-type symptoms disappeared in all 3 of these patients. The others were able to continue their work by using protective gloves. Respiratory symptoms were relieved by changing to non-powdered persulfate formulae.

A standard prick test series of common environmental allergens was performed in all 7 patients and patch tests with a standard and a hairdressers' series (including 2.5% ammonium persulfate, Chemotechnique, Malmö, Sweden) was performed in 6 patients. 5 of the patients had an atopic diathesis with positive reactions to common environmental allergens on prick testing. On patch testing, 2 of the patients had positive reactions to nickel, 1 to chromate and 2 to ammonium persulfate (Table 1).

Open application of 5% persulfate solutions to healthy skin was performed in 4 patients with skin symptoms, and 3 out of them had contact urticaria within 15 min (Table 1). The test was made 14–44 months (median 39 months) after the initial positive prick test. 20 control patients were negative on open application with 5% persulfate salts.

The patient without skin symptoms had given the blood sample for specific IgE but refused provocation studies. 1 patient could not be tested because of dermatographism, and 1 patient could not be found.

The sera of 5 patients were investigated with immunospot and RAST 0–44 months (median 39 months) after the initial positive prick test. On immunospot, specific binding of IgE to HSA-conjugated ammonium and potassium persulfates was found in 2 patients (Table 1) (Fig. 1). These 2 patients also had positive urticarial reactions to the open application test with both ammonium and potassium persulfate solutions. Specific binding of IgE to non-conjugated persulfates or pure HSA could not be demonstrated in these 5 patients. On RAST, specific binding of IgE to HSA-conjugated ammonium persulfate (0.5 PRU/ml, RAST class 1) was demonstrated in 1 patient, who was also clearly positive on immunospot (Fig. 1). No specific binding was demonstrated from the control sera.

Discussion

In 1963, Calnan and Shuster stated that immediate-type reactions to ammonium persulfate were more frequent than delayed-type reactions to the

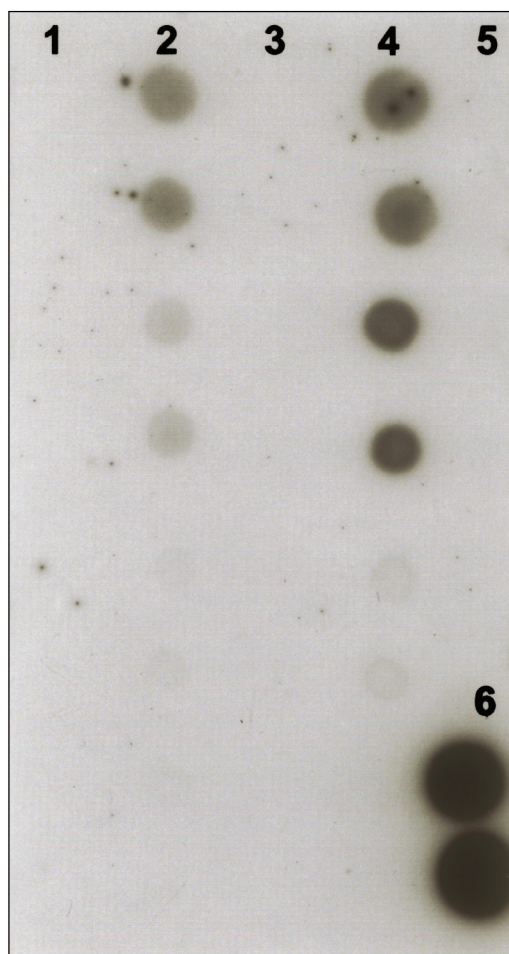


Fig. 1. Serum immunoglobulin E (IgE) to persulfates from patient no. 4 in Table 1. Dilutions of ammonium persulfate (1), ammonium persulfate-human serum albumin (HSA) (2), potassium persulfate (3), potassium persulfate-HSA (4), HSA (5) and birch pollen control (6).

same substance (4). Allergic contact dermatitis from ammonium persulfate is recognized amongst hairdressers (15–17). In our study, positive prick tests to persulfates were not rare in hairdressers. In fact, during the same 4-year period, we had no more cases of allergic contact dermatitis other than the 2 cases presented in this report, hence, immediate hypersensitivity happened to be much more common during that time. This is in accordance with the experience of Calnan and Shuster (4). The use of very fresh persulfate solutions may be important in detecting such immediate hypersensitivity.

Positive skin provocation supports the relevance of the positive prick test in patients with skin symptoms. In the present study, 3 patients out of 4 tested had urticarial reactions on open application to healthy skin. The patient with negative skin application had had widespread urticaria when his own hair was bleached. In

this case, the positive prick test was probably relevant in spite of the negative skin provocation. Persulfates are used in hair bleaches at concentrations up to 22% (18). A higher concentration of persulfate in the skin provocation (4, 5) might produce urticarial reactions more often than the 5% concentration that we used.

The severest immediate reactions have occurred in hairdressers' clients or consumers bleaching their hair at home (1, 4, 5, 11). Hairdressers with immediate hypersensitivity, in turn, often present with respiratory symptoms and milder skin symptoms such as local urticaria or hand eczema (5, 7, 9, 13). The symptoms of our patients were similar. Only 1 of them had severe angioedema and contact urticaria at work. 4 of our patients had hand eczema. Contact allergy to ammonium persulfate, atopy and irritant factors in hairdressers' work was probably more important factor contributing to their hand eczema than immediate persulfate hypersensitivity. Although immediate hypersensitivity usually produces only minor skin symptoms in hairdressers, these patients are at risk of widespread reaction when their own hair is bleached (4).

There is only 1 previous report of a positive ammonium persulfate RAST (9), and this contains no description of the RAST method or results in control patients. In the present study, we could demonstrate specific binding of IgE by 2 methods, RAST and immunospot. Immunospot showed specific binding of IgE to both ammonium and potassium persulfate HSA-conjugates in 2 patients. The other patients and the nonatopic control sera showed weak binding to HSA conjugates, which was concluded to be non-specific. 1 immunospot-positive patient also had a positive RAST to ammonium persulfate-HSA conjugate. Different binding properties of the solid-phase materials may have been the cause of the divergent results in the IgE-binding studies. Another reason may have been the low solubility and the use of frozen-stored stock solutions in RAST studies. In any case, distinct binding of IgE to both persulfate HSA conjugates was demonstrated on immunospot.

We gathered our patients from prick test files of 4 years. This explains why the median time interval between evaluation and the initial positive prick test was so long. After the positive prick test, the patients had stopped working or started to protect their skin from contact with hair bleaches. It is possible that specific IgE could be demonstrated more often, if the blood samples had been taken a few months after the presenting symptoms.

In conclusion, we could demonstrate specific binding of IgE to persulfates by 2 methods,

immunospot and RAST. The mechanism of immediate hypersensitivity to persulfates seems to be IgE-mediated at least in some patients.

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