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Anaphylaxis and severe systemic reactions caused by skin contact with persulfates in hair-bleaching products

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Summary

Background. Persulfates have been reported to cause both delayed-type and immediate skin reactions. They may also cause immediate reactions of the mucous membranes of the bronchial system through inhalation, leading to asthma and rhinitis. Anaphylactic reactions caused by contact with persulfates are rare. The mechanism of immediate reactions caused by persulfates is unclear.

Objectives. To report 2 cases with systemic reactions after skin contact with persulfates, and to propose a test protocol for diagnosing immediate reactions caused by persulfates.

Methods. Prick tests with serial dilutions of ammonium and potassium persulfate were performed. Patch tests were also performed with the two agents. Persulfate-specific IgE was detected with two different IgE immunoblotting techniques.

Results. Prick tests were positive with ammonium and potassium persulfate, but no specific IgE was detected in the serum. Patch tests showed early positive reactions to both persulfates in 1 patient.

Conclusions. Prick tests and patch tests can be valuable in the testing of patients with a suspicion of an immediate-type reaction caused by persulfates. The mechanism of these reactions remains unclear.

Key words: ammonium persulfate; anaphylaxis; asthma; potassium persulfate; specific IgE; urticaria.

Ammonium persulfate (CAS 7727-54-0), potassium persulfate (CAS 7727-21-1) and sodium persulfate (CAS 7775-27-1) are strongly oxidizing inorganic salts (1–3). Persulfates are widely used in different manufacturing processes in the textile, chemical, metallurgic, pharmaceutical, photographic, food and, particularly, cosmetic industries (2, 4). They are also used in hair-bleaching products and hair-colouring preparations to accelerate

the bleaching process, thus reducing the amount of peroxide used (1–3, 5). In addition to the bleaching products, consumers may be subjected to contact with persulfates in dental prosthesis cleansers (2).

Persulfates have been reported to cause both delayed-type and immediate skin reactions, including allergic contact dermatitis, irritant contact dermatitis, localized contact urticaria, and generalized urticaria (3, 4). Besides skin reactions, persulfates may cause immediate reactions in the mucous membranes of the bronchial system through inhalation, leading to asthma and rhinitis (6–8). Anaphylactic reactions caused by contact with persulfates are rare (9). However, the mechanism of immediate reactions caused by persulfates remains unclear. Although it has been speculated that these reactions are based on an immunological mechanism, persulfate-specific IgE cannot be detected in all patients.

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We report 2 cases with severe systemic reactions because of skin contact with persulfates in hair-bleaching products. The first case had anaphylaxis, and the second case had severe asthma. In addition, we have also reviewed the published case reports of severe systemic reactions caused by skin contact with persulfates. We propose a test protocol for diagnosing severe immediate reactions to persulfates, and discuss the value of patch testing in these cases.

Materials and Methods

Patients

Case 1. A 48-year-old woman had used bleaching products and hair dyes every 6 weeks, without any problems, for several years. She had a history of atopic dermatitis and rhinitis, but not of allergic contact dermatitis. She developed pruritus affecting the scalp 10 min after the application of a new hair-bleaching product by her hairdresser. Several minutes later, she developed erythema and oedema on her head, chest, and arms. She also felt increasingly dizzy. Although the hairdresser washed out the bleaching product, the subject became unconscious, with increased heart rate and low blood pressure, 45 min after the initial application of the new hair-bleaching product. She required resuscitation with adrenalin, dexamethasone, clemastine, and saline, and was transferred to a hospital, where the diagnosis of anaphylaxis was established. The day after the anaphylactic reaction, she went back to the hairdresser because her hair had acquired an orange colour after washing out of the hair-bleaching product earlier than prescribed. A permanent hair dye was applied, without any manifestation of symptoms. The hair-bleaching product that was used on the day of the anaphylactic reaction contained persulfates and hydrolysed wheat protein. No permanent hair dye was used that day or in the previous 6 weeks. Other products that were used on the day of the anaphylactic reaction, such as hair-styling products and shampoos, were used before and after the anaphylactic reaction, without causing any problems. After the anaphylactic reaction, the patient used hair dyes every 6 weeks without problems.

Case 2. A 36-year-old hairdresser had a history of asthma and rhinitis provoked by the use of bleaching products in the hair salon. She also reported contact urticaria after skin contact with bleaching products. There was no history of atopic dermatitis or allergic contact dermatitis. She wanted her hair to be washed by a colleague, and reclined her neck on the sink. Several minutes later,

she developed an urticarial reaction in the neck, facial oedema, erythema, and severe dyspnoea. At the hospital, she was diagnosed with severe asthma; she was treated with oxygen and adrenalin, and admitted overnight for observation. There were probably residual traces of a bleaching product on the sink after handling of an earlier client. The hair-bleaching product that was used in the hairdresser's salon contained persulfates. She had to leave her job as a hairdresser, because of the urticaria and the severe asthmatic complaints that she suffered every time a bleaching product was used in the salon. She has had no asthmatic symptoms since leaving her job.

Test procedures

We performed allergy tests in both of the cases, starting with prick tests. Prick tests were performed 11 months after the anaphylactic reaction in the first patient, and 3 months after the severe systemic reaction in the second patient.

Serial dilutions of freshly prepared ammonium and potassium persulfate (0.1%, 1.0% and 2.0% in aqua) were used. All tests were started with the lowest concentration, and this was raised until a positive reaction was observed. No further prick tests were performed once a positive reaction was observed. We started with prick-to-prick tests, in which only a very small amount of the dilution was brought under the skin surface by pricking the skin after dipping the needle in the dilution (10). Subsequently, we performed prick tests if prick-to-prick tests gave negative results. In the prick tests, a small amount of the dilution was placed on the forearm, and the skin was pricked. If there was still no positive reaction, intradermal tests were performed. This involved injecting 0.03 ml of the dilution into the forearm, producing a papule of 3–4 mm. Sufficient space was kept between the tested skin areas in all of the tests (10). Histamine served as a positive control and a saline solution served as a negative control in the prick tests. The prick test was regarded as positive when the size of the wheal was at least 80% of the positive control.

Subsequently, we performed patch tests with the European baseline series (TRUE Test®; Mekos, Hillerød, Denmark), cosmetic series (Trolab®, Hermal, Reinbek, Germany and Chemotechnique Diagnostics, Vellinge, Sweden), perfume series (Chemotechnique Diagnostics), and hairdresser's series (Trolab® and Chemotechnique Diagnostics, which included potassium persulfate 2.5% aqua and ammonium persulfate 2.5% petrolatum), in Van der Bend® square chambers (Van der Bend®, Brielle, The Netherlands) on Fixomull® stretch (BSN, Almere,

The Netherlands). The tests were read after 20 min and after 1 hr to assess an immediate reaction. In addition, the patch tests were read according to the guidelines of the International Contact Dermatitis Research Group on days 3 and 7.

The serum of the second patient, which was taken 3 months after the severe systemic reaction, was examined by IgE immunoblotting to detect persulfate-specific IgE. Paper discs, covalently coupled with ammonium sulfate [through human serum albumin (HSA)], were obtained from EUROIMMUN AG (Lübeck, Germany). After a washing step, these discs were incubated for 1 hr at 37°C with 50 µl of the patient's serum or with two sera with high levels of specific IgE against inhalant allergens. After a washing step, the discs were incubated at 37°C for 1 hr with 50 µl of mouse anti-human IgE (BD Biosciences, New York, USA). After a washing step, the discs were incubated for 1 hr at 37°C with 50 µl of rabbit anti-mouse IgG conjugated with horseradish peroxidase (Dako Denmark A/S, Glostrup, Denmark). After application of luminol, the chemiluminescence intensity was measured (Chemidoc TM XR; Bio-Rad Laboratories, Hercules, CA, USA). Additionally, IgEs against ammonium and potassium persulfate were measured as described by Aalto-Korte and Mäkinen-Kiljunen (2). Briefly, after the haptenization process, the HSA–persulfate conjugates were applied in three-fold dilutions (undiluted, and diluted $\times 5$ and $\times 25$) to nitrocellulose strips (5 µl per spot) and dried. After a washing step with phosphate-buffered saline (PBS), the strips were blocked by incubation with 3% bovine serum albumin in PBS for 1 hr at room temperature. After the blocking step, the strips were incubated with the patient's serum or control sera, as described for the paper discs.

Results

Case 1

The prick test with histamine as positive control showed a wheal of 7 mm and flare. Prick-to-prick tests and prick tests with the serial dilutions of both persulfates gave negative results. The intradermal tests gave positive results (wheal and flare) after 15 min for ammonium persulfate 0.1% aqua (wheal of 20 mm) and potassium persulfate 0.1% aqua (wheal of 14 mm) (Fig. 1). Several hours after the intradermal tests, the patients developed dizziness, which cleared after she took antihistamines. Intradermal tests with ammonium and potassium persulfate 0.1% gave negative results in 4 controls.

No patch test reactions were observed after 20 min and 1 hr. On days 3 and 7, patch testing showed a 1+ positive reaction for ammonium persulfate 2.5% pet. and nickel sulfate. Specific IgE against wheat protein was negative.

Case 2

The prick test with histamine as positive control showed a wheal of 6 mm and flare. Prick-to-prick tests gave positive results (wheal and flare) for both ammonium persulfate 1.0% aqua (wheal of 8 mm) and potassium persulfate 1.0% aqua (wheal of 9 mm) (Fig. 2). Dyspnoea occurred 10 min after the prick-to-prick tests. It cleared after inhalation of β_2 -sympathomimetics. Prick-to-prick tests with ammonium and potassium persulfate 1.0% gave negative results in 4 controls.

Patch tests showed a positive reaction after 20 min for both ammonium persulfate 2.5% pet. and potassium persulfate 2.5% aqua, producing a wheal of more than 12 mm and flare (Fig. 3). The results could not be read after 3 and 7 days, because these two patches had

Fig. 1. Positive intradermal test results with ammonium persulfate 0.1% aqua and potassium persulfate 0.1% aqua in case 1.

Fig. 2. Positive prick-to-prick test results with ammonium persulfate 1.0% aqua and potassium persulfate 1.0% aqua in case 2.

Fig. 3. Positive reaction to ammonium persulfate 2.5% pet. after 20 min in case 2.

been removed. On days 3 and 7, patch testing showed a 1+ positive reaction for nickel sulfate, neomycin, epoxy resin, *Myroxylon perei*, methyldibromo glutaronitrile, 2-bromo-2-nitropropane-1,3-diol, hydroxyisohexyl 3-cyclohexene carboxaldehyde, fragrance mix II, thioglycolic acid, and thiolactic acid.

Both tests for the measurement of IgE against persulfates in the patient's serum gave negative results. The total IgE level was 704 kU/l, and the differential leukocyte count showed 2.9% eosinophils.

The patient was referred to a respiratory physician, who concluded that she had allergic asthma because of sensitizers in the hairdresser's salon. No specific inhalation challenge (SIC) with persulfate salts was performed. Her asthmatic complaints disappeared after she left her job as a hairdresser.

Discussion

An anaphylactic reaction caused by immediate hypersensitivity to persulfates after application of a hair-bleaching

product is described in the first case reported here. This was confirmed by the positive intradermal test results with ammonium and potassium persulfate. Patch tests also showed a delayed-type reaction to these persulfates. The hair-bleaching product that was used contained a hydrolysed wheat protein. Allergen-specific IgE against wheat protein in her serum was negative, making anaphylaxis caused by wheat hydrolysates unlikely.

Well-documented anaphylactic reactions because of persulfates are rare in the current literature. In 2005, Babilas described a hairdresser who acquired allergic contact dermatitis following contact with bleaching substances (9). This dermatitis disappeared after she changed her profession, but, upon private use of a bleaching product, she suffered a severe anaphylactic reaction with unconsciousness. In 1972, Brubaker described a patient who used a bleaching product in the usual manner (11). After several minutes, she developed pruritus on the face, swelling of the upper body, and difficulty in breathing. In the hospital, she had symptoms of shock with generalized erythema and urticaria, with good responses to oxygen and intravenous adrenalin. Although this reaction is similar to the symptoms that we have described in our first case, it is not clear whether an anaphylactic reaction was diagnosed. There are no other studies describing anaphylaxis after contact with persulfates. There are several studies describing systemic reactions, especially asthma, after contact with persulfates (6, 9). In 2000, Perfetti et al. described a hairdresser with a history of occupational asthma, rhinitis and urticaria caused by ammonium persulfates (6). This patient developed an anaphylactoid reaction after patch testing with ammonium persulfate.

Our second case was a hairdresser with contact urticaria, and occupational asthma and rhinitis, after exposure to a bleaching product, caused by immediate

hypersensitivity because of persulfates. This was confirmed by the positive prick-to-prick test results and an early reaction on patch testing with both ammonium and potassium persulfate. Although hairdressers have a risk of developing occupational asthma and rhinitis, in which persulfates are the major agents involved (7), we found no other articles describing this type of severe reaction after contact with only a small amount of persulfate. The gold standard test for the diagnosis of occupational asthma and identification of the possible causal agent is the SIC (11). The SIC was not performed in our patient.

Patients who have had an allergic reaction to persulfates must avoid hair-bleaching products. Hair-bleaching products and hair-colouring preparations must be checked every time before use, because ingredients may be different and cause a life-threatening situation. Persulfates have several synonyms, which makes it more difficult to avoid them (3, 8). The second patient had to leave her job as a hairdresser because of the severe asthmatic and rhinitis complaints when she was working in the hair salon. In patients with less severe bronchial reactions to persulfates, there is a possibility of using non-powdered forms of bleaching products with a decreased risk of inhalation. Gloves must be used to prevent direct contact with persulfates, and good ventilation is necessary to decrease the risk of inhalation. Hairdressers with a history of only minor skin symptoms after contact with persulfates are at risk of widespread reactions when their own hair is bleached (2). Urticarial reactions after direct skin contact or inhalation of persulfates seem to occur principally in asthmatics (6).

Prick and patch testing

When there is a suspicion of an immediate reaction to persulfates, prick tests and patch tests can be performed. Given the fact that these tests may cause (severe) systemic reactions, a reliable test protocol is required. In 2003, Aalto-Korte and Mäkinen-Kiljunen recommended the use of concentrations of 2% for prick testing, and stated that the use of freshly prepared solutions may be important to detect immediate reactions (2). As we showed in our second case, a positive reaction can already be obtained by a prick-to-prick test with a concentration of 1.0%. We would recommend the use of serial dilutions (0.1%, 1.0%, and 2.0%) and starting with prick-to-prick tests, followed by prick tests if the former give negative results. If no positive reaction is seen, intradermal tests can be performed. When there is no positive reaction with either of these tests, immediate hypersensitivity to persulfates seems to be unlikely, although the sensitivity and the specificity of prick tests with persulfates are not known.

It is important to realize that the severity of the reaction in the patient does not seem to correlate with the concentration used in the prick tests. In our case reports, the first patient with an anaphylactic reaction had no positive reaction in prick-to-prick tests and prick tests, whereas the second patient with asthma, rhinitis and urticaria already had a positive reaction at a low concentration in the prick-to-prick test.

Patch tests are normally used to detect delayed hypersensitivity to persulfates, but early reactions may also be observed when they are read after 20 min or 1 hr. Babilas in 2005 (9) and Perfetti et al. in 2000 (6) described early reactions of patch tests in patients with urticarial and/or asthmatic complaints after contact with persulfates. Patch tests can be used when prick tests are not available or when a patient is suspected of having combined immediate and delayed reactions to persulfates (8). It is important to use freshly prepared solutions, because persulfates are highly unstable in aqueous solution (2, 8). The patient should be monitored carefully, and the skin beneath the patches should be checked regularly after application of the test chambers. The patches must be removed when any symptom occurs. It is practical to use transparent chambers. Upon leaving the hospital after patch tests or prick tests, the patient must be urged to seek medical aid should additional symptoms occur. One may consider whether prick tests are necessary when an early reaction is observed in patch tests. However, the results of prick tests are more reliable than those of patch tests after 20 min and 1 hr. Moreover, prick tests are safer, because of the serial dilutions and the successive use of different methods (prick-to-prick followed by prick test). Therefore, in patients with severe reactions and generalized urticaria, we recommend starting with prick tests. In patients with localized urticaria, patch test results after 20 min may be sufficient.

Allergen-specific IgE

When a positive prick test result or an early reaction in a patch test is seen, the question remains of whether these reactions are immunological or caused by the release of histamine via a direct action on the mast cells. The fact that some people already react upon the first exposure to the bleaching product argues against an immunological mechanism. The finding that only a small number of people are affected is in favour of the immunological mechanism and against the direct action on the mast cells (12). In our study, none of the controls showed a positive reaction in prick tests, which indicated specific sensitization. If immediate reactions to persulfates are

based on an immunological reaction mediated by specific IgE, then this specific IgE should be detectable in the sera of the patients. We tried to detect this persulfate-specific IgE with two different IgE-immunoblotting techniques, but without success. In the current literature, persulfate-specific IgE is reported in only two studies. Brauel et al. in 1995 reported a positive IgE test result with ammonium persulfate in a patient with contact urticaria, rhinitis, and asthma (13). Aalto-Korte and Mäkinen-Kiljunen in 2003 investigated 138 patients with a suspicion of allergic symptoms caused by contact with hair cosmetics by using 2% solutions of ammonium and potassium persulfate in prick tests (2). Seven patients (all of them hairdressers) had positive reactions to at least one persulfate salt. The sera of 5 patients were investigated with immunospot and specific IgE assay 0–44 months after the initial positive prick test results. Persulfate-specific IgE was detected in only 2 of these patients. There may be several reasons why persulfate-specific IgE could not be detected. If the time between exposure to the persulfates and collection of sera is too long, IgE levels may be below detectable levels (2). The IgE immunoblot may be false-negative because of the lack of a standardized method for the detection of specific IgE against the haptenized persulfates. However, the IgE

test with the commercially available ammonium persulfate paper discs also gave a negative result. Unfortunately, we did not have a positive control serum with a detectable level of IgE against persulfates in order to check whether the test procedure was valid. Finally, it may be that the immediate reactions to persulfates are not IgE-mediated in all patients. However, further research is needed to verify whether this is true.

In conclusion, we report 2 cases of severe systemic reactions and anaphylaxis after contact with persulfates. Although persulfates are known to cause delayed and immediate reactions, anaphylaxis is rare. A good test protocol is required to test patients with a suspicion of immediate hypersensitivity to persulfates. We recommend the use of serial dilutions and starting with prick-to-prick tests. In patients with localized urticaria, patch test results after 20 min may be sufficient. The mechanism by which persulfates causes these immediate reactions remains to be fully elucidated.

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