

Letter to the Editor

Ortho-phthalaldehyde-induced anaphylaxis after laryngoscopy

To the Editor:

In August 2005, a 25-year-old woman was referred to our outpatient clinic for evaluation of a surgical indication for a vocal cord papilloma. She had undergone once-a-month check-ups by laryngoscopy for the previous 5 months. On the day of her first visit to our hospital, an anaphylactic reaction occurred, with dyspnea, runny nose, systemic urticaria, tachycardia, and a mild decrease in the blood pressure at the end of a laryngoscopic examination. The anaphylaxis was brought under control by administration of epinephrine, hydrocortisone, and chlorpheniramine.

Two weeks after the anaphylaxis, a search for the causal agent was performed. She had cedar pollen rhinitis but no history of asthma or atopic eczema. Her serum IgE was mildly elevated (340 IU/mL). After informed consent was obtained, skin tests and challenge tests were performed for latex and the local anesthetics used during the laryngoscopic procedure, but no local or systemic allergic reactions were observed. We next focused on a disinfectant solution containing 0.55% ortho-phthalaldehyde (OPA) that was routinely used for pretreatment of the laryngoscope at both the previous hospital and our hospital. The solution showed a positive reaction in an intracutaneous test at a 1:1000 dilution (wheal of 6×6 mm and flare of 22×15 mm) at 15 minutes, which lasted for more than 24 hours. Four healthy volunteers had a negative result to this test. These results suggested that the disinfectant was the cause of her symptoms, via either an immunologic or, with a remote possibility, an irritant reaction. Accordingly, subsequent laryngoscopic examinations were performed using an OPA-disinfected, thoroughly rinsed fiberoptic, and the patient showed no allergic symptoms.

A histamine release test using the patient's basophils was performed. Briefly, basophils were exposed to serial dilutions of the OPA-containing disinfectant and pure OPA solution (original concentration of OPA in both solutions: 0.55%) in a buffer containing 0.03% human serum albumin. It revealed that both the disinfectant and pure OPA solution evoked obvious release of histamine (Fig 1, A), but no release was observed for basophils from 3 healthy control donors. Next, sensitization experiments were performed; basophils from healthy subjects were treated at 4°C for 5 minutes with acetate buffer (pH 3.7) to remove surface-bound IgE, sensitized at 37°C for 2 hours with the patient's serum and then exposed to OPA. As a result, after sensitization with the patient's serum, basophils from the control donors released histamine in response to OPA, although they did not release histamine when the patient's serum was heated for 2 hours at 56°C before use (Fig 1, B). These results clearly demonstrated that the patient's anaphylaxis was mediated by OPA and IgE in her serum.

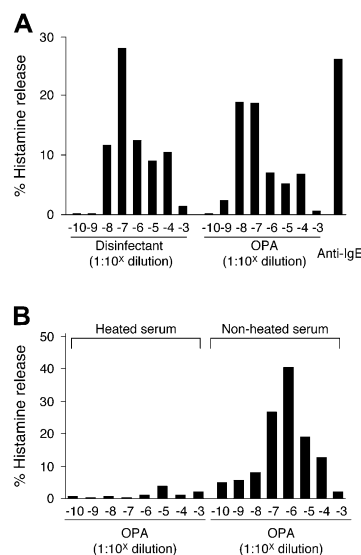


FIG 1. A, Histamine-release tests using the patient's basophils. The histamine in the supernatant was measured. Anti-IgE antibody at 14 μ g/mL was used as a positive control stimulus. Data are representative of 2 separate experiments. **B,** Histamine release tests of basophils sensitized with the patient's serum. Data are the mean values of 3 separate experiments.

This is the first report of anaphylaxis following OPA-disinfected laryngoscopy. Skin tests and *in vitro* histamine release tests were useful for identifying the allergen in this case. Based on our *in vitro* findings, the participation of OPA-specific IgE antibody in the pathogenesis of the anaphylaxis is strongly indicated. This patient had been sensitized before referral to our hospital, presumably by repeated exposure to trace amounts of OPA remaining on the fiberoptic. Importantly, extensive rinsing (>15 minutes) of the fiberoptic decreased the amount of residual OPA below the threshold level capable of triggering an anaphylactic response in this patient.

Ortho-phthalaldehyde is a recently developed disinfectant.¹ This compound has several advantages compared with the commonly used glutaraldehyde, including high stability over a wide pH range, and a negligible level of evaporation, leading to a lower risk of mucosal irritation in medical workers.² However, OPA is a low-molecular-weight substance and can probably act as a hapten after conjugation to carrier proteins, presumably in a similar fashion to glutaraldehyde.³ In our histamine release test, we assume that OPA was haptenated to a constituent protein (eg, albumin) in the test system, enabling it to elicit histamine release from the basophils. Recently, Sokol⁴ reported 4 patients demonstrating anaphylaxis after cystoscopy and positive skin prick tests for OPA. That report and the present case collectively suggest that repeated exposure to OPA-disinfected equipment can sensitize some patients, and that OPA can rarely cause IgE-mediated anaphylaxis in

sensitized subjects. Allergists thus need to be aware of such potential allergens to which patients may be exposed in routine medical procedures.

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