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## Periorbital Edema After Atracurium Administration

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Atracurium produces little or no cardiovascular effects from histamine release.<sup>1,2</sup> However, anaphylaxis,<sup>3</sup> bronchospasm,<sup>4</sup> and local skin reactions<sup>5</sup> have been described following its use. We describe a case of periorbital edema following the administration of atracurium.

### REPORT OF A CASE

A 10-yr-old female (40 kg) presented for strabismus repair of her right eye on 5/13/86. The patient had undergone general anesthesia on three previous occasions without any complications. Three months prior to the current surgery, she received meperidine (2 mg/kg iv) and diazepam (0.25 mg/kg iv) during a colonoscopy and developed hives around the iv site. There was no associated bronchospasm or hypotension. Although there was a positive family history of atopy, the patient's mother stated that her daughter had no hayfever, asthma, or food or drug allergies.

On the day of surgery, the patient was not premedicated, and anesthesia was induced with thiopental (5 mg/kg iv) and 50% nitrous oxide in oxygen. Atracurium (0.5 mg/kg iv) was then administered over 30 s to facilitate endotracheal intubation. Thirty to 45 s after administration of these drugs, and following intubation, facial flushing was evident. Within 4 min, during the administration of isoflurane (1.5%), flushing progressed to the arms and upper chest with associated periorbital and conjunctival edema. Within 15 min, severe periorbital, conjunctival, and lid edema were present in spite of the administration of 30 mg of iv diphenhydramine. Vital signs were stable throughout this period, and there was no evidence of bronchospasm. Anesthesia was maintained with 50% nitrous oxide in oxygen and 1.5% isoflurane.

The surgeons decided not to proceed with the strabismus repair because the periorbital edema would make it a technically difficult

procedure. Laryngoscopy was performed prior to extubation and revealed mild pharyngeal and vocal cord swelling that was treated with nebulized racemic epinephrine in the recovery room. Although flushing and conjunctival edema persisted for several hours, there was no evidence of respiratory distress or stridor. The patient was observed overnight in the recovery room because of the potential for recurrence of the laryngeal edema. Following an uneventful night, she was discharged. Periorbital edema persisted for 7-8 days.

One month later, the patient returned for further investigation of the cause of the reaction and the drug responsible. Intradermal testing of thiopental and atracurium was performed according to Fisher's protocol.<sup>6</sup> Histamine (.01%) and 0.9% saline were used as controls. The injection of histamine (0.01 ml) produced a 3-mm wheal and flare, while the injection of saline produced no response.

Immediately prior to testing, thiopental (2.5% solution) and atracurium (10 mg/ml) were diluted by injection into preservative-free normal saline. The dilutions used were atracurium 1:1000, 1:100, and thiopental 1:1000, 1:100. Skin responses were read 30 min after intradermal injection of sufficient solution to raise a 1-2-mm wheal. Injection of thiopental produced no response, while both dilutions of atracurium produced responses greater than that of the histamine control. Atracurium 1:1000 triggered a 7-mm wheal and atracurium 1:100 a 9-mm wheal, both persisting for more than 60 min.

### DISCUSSION

This patient's positive intradermal reaction to atracurium 1:1000 suggests a type I hypersensitivity reaction. Although a positive intradermal reaction is usually greater than or equal to 1.0 cm, a wheal of 7 mm can be considered positive if it persists longer than 30 min and is greater than the wheal produced by the control.<sup>7</sup> However, a type I hypersensitivity reaction requires previous exposure to the drug and classically involves IgE antibodies bound to mast cells.<sup>8</sup> Thus, the mechanism of sensitization in this patient is unknown, as two of the previous general anesthetics occurred prior to the availability of atracurium and the third involved administration of succinylcholine, pancuronium, isoflurane, and thiopental. Her sensitization may be related to the previously reported phenomenon of crossed anaphylaxis.<sup>9-13</sup> Some patients develop antibodies to muscle relaxants to which they have not been

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exposed because of contact with other substances that also contain quarternary ammonium groups, *e.g.*, disinfectants, cosmetics,<sup>11</sup> or previously administered neuromuscular blocking agents. In the present case, sensitization to atracurium may have occurred through previous exposure to pancuronium or succinylcholine. The quaternary ammonium radical constitutes the molecular basis of this phenomenon and, thus, the allergy is not specific to a particular muscle relaxant. With this consideration in mind, we requested that the patient return for further testing before her next general anesthetic, because of the possibility of allergy to multiple muscle relaxants.

At present, intradermal testing is the most reliable way of diagnosing allergic reactions to anesthetic agents.<sup>7</sup> Although sequential complement measurement is more specific than intradermal testing, it was not performed in this patient because it does not indicate the drug responsible for a specific reaction.<sup>8</sup> Furthermore, significant complement conversion may not occur in the absence of a systemic reaction.<sup>14</sup> Patch, skin prick, and passive transfer tests reportedly also add little to the value of intradermal testing.<sup>7</sup> In the presence of a drug that is capable of releasing histamine on its own, the definitive method for implicating an immune mechanism would be demonstration of IgE antibodies by means of radioimmunoassay, a method already tested with succinylcholine.<sup>13</sup>

In the present case, direct pharmacologic release of histamine cannot be ruled out. The drug was administered over 30 s, and the recommendation of the manufacturer is 60 s in atopic individuals. The absence of hypotension at the height of the reaction is difficult to explain; it may reflect our inability to detect the transient drop in blood pressure that might occur during a mild hypersensitivity response mediated through histamine or immune mechanisms. The prolonged persistence of the periorbital edema, however, may be related to a late-phase skin reaction similar to that reported with IgG antibody in ragweed allergy, the mechanism for which is an inflammatory infiltrate with eosinophils following an IgG-mediated reaction.<sup>15</sup>

In summary, our patient experienced an adverse reaction to atracurium. Further studies may be indicated

to elucidate the incidence and mechanism of such reactions.

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