

IgE-mediated allergy to remifentanyl?

Wei-I Lee¹, Melinda C Ford^{2,*} and Katrina L Randall^{1,3,*}

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Remifentanyl is an ultra-short-acting synthetic opioid receptor agonist that belongs to the class of phenylpiperidines.¹ Reports of hypersensitivity reactions to remifentanyl are rare. An eight-year national survey from France reported that remifentanyl allergy accounted for <0.08% of 2516 patients with suspected intraoperative hypersensitivity.² Here, we report a case of perioperative urticaria, which likely represented an IgE-mediated reaction to remifentanyl. The patient's written consent for publication was obtained.

A previously well man in his thirties was referred by an anaesthetist to be assessed in the anaesthetic allergy clinic at our institution. He had undergone a right shoulder arthroscopy and synovectomy four months prior, and was noted to have an urticarial rash involving his torso and arms at the end of his surgery. He did not have cardiorespiratory compromise, and the rash settled over the next 60–120 min. Intraoperatively he had received rocuronium, propofol, midazolam, fentanyl, remifentanyl, morphine, parecoxib, dexamethasone, granisetron, sugammadex and cephazolin. The referring anaesthetist suspected cephazolin or sugammadex as the causative agent as his rash appeared soon after these two drugs were given. His tryptase level was not tested in the immediate postoperative period.

He had had three previous shoulder surgeries, a vasectomy and wisdom teeth extraction; there were no issues reported from these surgical procedures. Apart from an unclear allergy to 'brown tape' many years before, he reported no other allergy or atopy. The patient reported no exposure to cough syrup since childhood.

The patient's blood tests revealed a baseline tryptase level within the normal range, and negative results for allergen-specific IgE to chlorhexidine, suxamethonium, pholcodine, morphine, latex and cefaclor. Skin prick testing to latex was negative. Skin prick, followed by intradermal testing, to rocuronium, cephazolin, sugammadex, propofol, fentanyl and morphine were also negative.

Skin prick testing to remifentanyl at the adult infusion concentration (0.05 mg/ml) was negative. This was followed by intra-dermal testing to a 1:100 dilution (remifentanyl 0.0005 mg/ml), which also gave a negative

result. However, intradermal testing at a 1:10 dilution (0.005 mg/mL) gave a positive result. This testing was done according to the recommendations of the Australian and New Zealand Anaesthetic Allergy Group in the presence of appropriate positive and negative controls.³ As this testing indicates IgE sensitisation, we felt that the most likely cause of the patient's urticaria had been an IgE-mediated reaction to remifentanyl. We have advised the patient that, should he require future anaesthesia, he should notify his anaesthetist of his likely remifentanyl allergy. We have also recommended that he obtain a Medication Allergy bracelet to this effect, as there is a possibility of a more severe reaction, including anaphylaxis, should the patient receive remifentanyl again.

The risk of a false positive skin test result exists, but the patient had no other evidence of dermatographism with his other testing, and the concentration used was one that had previously been published as non-irritant in normal controls.⁴ Unlike other opioids, fentanyl and remifentanyl do not cause direct mast cell activation.⁵ The only way to determine definitively if this were a false positive reaction would be an intravenous challenge, but we felt that the benefit would not outweigh the risk, as there are other anaesthetic and analgesic options available for his future anaesthesia if required.

Although neuromuscular blocking drugs, latex, antibiotics and chlorhexidine are the most common causes of perioperative hypersensitivity reactions,^{2,6} clinicians also need to consider testing for rarer possibilities such as remifentanyl in the event that an allergic reaction is observed, so that patients can be advised appropriately for future anaesthetics.

¹Department of Immunology, The Canberra Hospital, Australia

²Department of Anaesthesia, The Canberra Hospital, Australia

³Australian National University (ANU) Medical School, Canberra, Australia

*These authors contributed equally.

Corresponding author:

Katrina Randall, Department of Immunology, The Canberra Hospital, Woden, ACT 2606, Australia.

Email: Katrina.Randall@anu.edu.au

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References

1. Song D and White PF. Remifentanyl as an adjuvant during desflurane anesthesia facilitates early recovery after ambulatory surgery. *J Clin Anesth* 1999; 11: 364–367.
2. Mertes PM, Alla F, Trechot P, et al. Anaphylaxis during anesthesia in France: an 8-year national survey. *J Allergy Clin Immunol* 2011; 128: 366–373.
3. Scolaro RJ, Crilly HM, Maycock EJ, et al. Australian and New Zealand Anaesthetic Allergy Group Perioperative Anaphylaxis Investigation Guidelines. *Anaesth Intensive Care* 2017; 45: 543–555.
4. Brockow K, Garvey LH, Aberer W, et al. Skin test concentrations for systemically administered drugs – an ENDA/EAACI Drug Allergy Interest Group position paper. *Allergy* 2013; 68: 702–712.
5. Blunk JA, Schmelz M, Zeck S, et al. Opioid-induced mast cell activation and vascular responses is not mediated by mu-opioid receptors: an in vivo microdialysis study in human skin. *Anesth Analg* 2004; 98: 364–370.
6. Low AE, McEwan JC, Karanam S, et al. Anaesthesia-associated hypersensitivity reactions: seven years' data from a British bi-specialty clinic. *Anaesthesia* 2016; 71: 76–84.