



Two severe perioperative hypersensitivity reactions in a single patient—a case report of a medication error

Iva Mikulic · Robert Likic · Ivana Cegec · Viktorija Erdeljic Turk · Matea Radacic Aumiler · Ksenija Makar Ausperger · Iveta Mercep

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Perioperative immediate hypersensitivity reactions are serious but rare clinical problems that require further evaluation for possible drug allergy. Hypersensitivity reactions and medication errors are types of adverse drug reactions. Here we present a case of two perioperative hypersensitivity reactions in a single patient due to hypersensitivity to neuromuscular blocking agents, the second of which was a medication error.

Background

Perioperative immediate hypersensitivity (POH) reaction is a life-threatening condition that requires rapid intervention and has a wide range of causes. The lack of a standardized protocol for testing POH culprit drugs is a major problem. Although the drug provocation test (DPT) remains the gold standard for hypersensitivity testing, it is not yet universally recommended in this setting because of the risk of pharma-

cologic effect. Nevertheless, it is routinely performed in some centres. [1].

We present a case of two POH reactions in a single patient due to hypersensitivity to neuromuscular blocking agents (NMBAs), the second of which was a medication error (ME).

Case representation

A 52-year-old woman was first evaluated in our department in June 2019 for POH. In September 2018, she suffered anaphylactic shock during induction in general anaesthesia for thyroid surgery after midazolam, propofol, sufentanil, and vecuronium were administered. The surgery was postponed, and she was referred to our centre for evaluation.

Skin prick tests (SPT) and intradermal (ID) tests to midazolam, propofol, sufentanil, rocuronium, and atracurium were performed. All SPT tests were negative and the ID test for rocuronium was positive while all other tests remained negative. The tests were performed according to the European Academy of Allergy and Clinical Immunology (EAACI) guidelines [1]. For skin tests maximal nonirritating concentrations for perioperative drugs advised by a European Network on Drug Allergy (ENDA)/EAACI Drug Allergy Interest Group were used [2]. SPTs were performed with undiluted midazolam (5 mg/ml), propofol (10 mg/ml), sufentanil (0.005 mg/ml) and rocuronium (10 mg/ml) and with atracurium (1 mg/ml) in 1/10 dilution. For IDT dilution of 1/10 was used for midazolam (0.5 mg/ml), propofol (1 mg/ml) and sufentanil (0.0005 mg/ml), 1/200 for rocuronium (0.05 mg/ml) and 1/100 for atracurium (0.01 mg/ml). Normal saline and histamine were used for negative and positive control.

An intravenous DPT with a small dose of drug with no pharmacological effect was further performed to

I. Mikulic, MD (✉) · R. Likic, MD, PhD · I. Cegec, MD · V. Erdeljic Turk, MD, PhD · M. Radacic Aumiler, MD, PhD · K. Makar Ausperger, MD, PhD · I. Mercep, MD, PhD
Department of Clinical Pharmacology, University Hospital Centre Zagreb, Zagreb, Croatia
ivakraljickovic@gmail.com

R. Likic, MD, PhD · I. Mercep, MD, PhD
Faculty of Medicine, University of Zagreb, Zagreb, Croatia

M. Radacic Aumiler, MD, PhD
Department of Biotechnology, University of Rijeka, Rijeka, Croatia

confirm a safe alternative. During the intravenous exposure the patient is under the close supervision of a physician trained in cardiopulmonary resuscitation for an hour and further monitored for 24 h at the ward. She was tested with intravenous DPT for midazolam (0.2 mg), propofol (0.5 mg), sufentanil (0.2 mcg), and atracurium (0.2 mg) one drug a day without developing an allergic reaction and was discharged with a detailed summary letter that included the list of drugs that were tested with both their generic and trade names.

Thyroid surgery was rescheduled for September 2019, and this time, midazolam, sufentanil, etomidate, and vecuronium of a different brand name were used. Again, the patient developed anaphylactic shock and the surgery was not performed.

She was admitted to our unit for the second time in November 2019. Again, SPT and ID tests were performed to etomidate (SPT 2 mg/ml, IDT 0.2 mg/ml), rocuronium, vecuronium (SPT 4 mg/ml, IDT 0.4 mg/ml), suxamethonium (SPT 10 mg/ml, IDT 0.1 mg/ml) and atracurium. All skin tests for rocuronium, vecuronium and suxamethonium were positive. Negative skin tests for etomidate and atracurium were followed by intravenous DPT, which were all negative. The dosage of etomidate used in DPT was 0.1 mg. The patient was found to be allergic to rocuronium, vecuronium, and suxamethonium, but not to atracurium.

Finally, the surgery was performed in January 2020 using midazolam, sufentanil and atracurium, without any complications.

Conclusion

During the initial evaluation and testing we had a temporary lack of vecuronium reagent and rocuronium was tested instead. Although this is a limitation of the study, results of the skin tests along with the patient history clearly indicated vecuronium and rocuronium cross-reactivity and vecuronium was considered the culprit. Not testing vecuronium did not influence the decision on what drugs to use in DPT, the conclusion and the further recommendations.

In the first surgery vecuronium Norcuron® from Merck Sharp & Dohme, Ljubljana, Slovenia was administered and in the second Vecurol from Demo A.B.E.E., Athens, Greece. This ME could have been prevented either by following the recommendation in the discharge letter or, as we strongly believe, by using generic instead of brand drug names in everyday practice.

We would like to stress the importance of clear communication between clinicians, the key factor being an accurate discharge letter. It should be structured to provide sufficient critical information in

a concise, understandable format with clear instructions and recommendations.

The appropriate drug hypersensitivity (DH) documentation is a crucial measure for the prevention of repeat exposure to the culprit drug. Using a standardized drug allergy passport and/or a drug allergy alert card to increase awareness of DH and minimize prescription errors is advised. The importance of always having the information on DH available should be emphasized to the patient [3].

Also, this report shows that confirmed cross-reactivity to aminosteroid NMBAs does not necessarily involve allergy to tetrahydroisoquinoline derivatives. When investigating hypersensitivity to NMBAs, it is possible to find a safe alternative.

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Conflict of interest I. Mikulic, R. Likic, I. Cegec, V. Erdeljic Turk, M. Radacic Aumiler, K. Makar Ausperger and I. Mercep declare that they have no competing interests. The authors have no relevant financial or nonfinancial interests to disclose.

References

- Garvey LH, Ebo DG, Mertes P-M, et al. An EAACI position paper on the investigation of perioperative immediate hypersensitivity reactions. *Allergy*. 2019;74:1872–84.
- Brockow K, Garvey LH, Aberer W, Atanaskovic-Markovic M, Barbaud A, Bilo MB, Bircher A, Blanca M, Bonadonna B, Campi P, Castro E, Cernadas JR, Chiriac AM, Demoly P, Grosber M, Gooi J, Lombardo C, Mertes PM, Mosbech H, Nasser S, Pagani M, Ring J, Romano A, Scherer K, Schnyder B, Testi S, Torres M, Trautmann A. Terreehorst I on behalf of the ENDA/EAACI drug allergy interest group. Skin test concentrations for systemically administered drugs—an ENDA/EAACI drug allergy interest group position paper. *Allergy*. 2013;68:702–12.
- Brockow K, Aberer W, Atanaskovic-Markovic M, Bavbek S, Bircher A, Bilo B, Blanca M, Bonadonna P, Burbach G, Calogiuri G, Caruso C, Celik G, Cernadas J, Chiriac A, Demoly P, Oude Elberink JNG, Fernandez J, Gomes E, Garvey LH, Gooi J, Gotua M, Grosber M, Kauppi P, Kvedariene V, Laguna JJ, Makowska JS, Mosbech H, Nakonechna A, Papadopolous NG, Ring J, Romano A, Rockmann H, Sargur R, Sedlackova L, Sigurdardottir S, Schnyder B, Storaas T, Torres M, Zidarn M, Terreehorst I. Drug allergy passport and other documentation for patients with drug hypersensitivity—an ENDA/EAACI drug allergy interest group position paper. *Allergy*. 2016;71:1533–9.