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SUCCESSFUL RE-EXPOSURE TO REMIMAZOLAM AND ROCURONIUM WITH PREOPERATIVE PROPHYLAXIS IN A HIGH-RISK PATIENT: A CASE REPORT

Donghyo Kim — Department of Anesthesiology and Pain Medicine, Daegu Fatima Hospital, 99 Ayang-ro, Daegu 41199, Korea

Jooneung Park — Department of Anesthesiology and Pain Medicine, Daegu Fatima Hospital, 99 Ayang-ro, Daegu 41199, Korea

Jihyang Lee — Department of Anesthesiology and Pain Medicine, Daegu Fatima Hospital, 99 Ayang-ro, Daegu 41199, Korea

ABSTRACT We report a case of a high-risk patient with a history of drug allergy who developed anaphylactic shock following induction with remimazolam and administration of rocuronium. During a subsequent surgery, preoperative prophylaxis with methysol and pheniramine was administered prior to re-exposure to the same agents. No anaphylactic reaction occurred, and anesthesia was successfully completed without complications. This case highlights the potential role of preoperative prophylaxis and structured perioperative planning in reducing the risk of recurrence in susceptible patients.

KEYWORDS : Remimazolam; Rocuronium; Perioperative Anaphylaxis; Preoperative Prophylaxis

INTRODUCTION

Anaphylaxis is generally an unanticipated severe allergic Perioperative anaphylaxis is typically an unexpected and rapidly developing severe hypersensitivity reaction that may arise during surgery, particularly when multiple anesthetic-related medications are administered simultaneously. (Hepner & Castells, 2003). Although its reported incidence is relatively low, the consequences can be catastrophic, including severe hypotension, cardiovascular collapse, bronchospasm, and even death. The diagnosis is particularly challenging in the anesthetized patient, as typical early signs of anaphylaxis may be masked or misinterpreted under general anesthesia. Reported mortality rates for immediate hypersensitivity reactions occurring during anesthesia range from approximately 3% to 9%, with variation among different countries. (Mertes et al., 2011). The reported frequency of immediate allergic hypersensitivity reactions during anesthesia differs across countries, with an estimated incidence ranging from 1 in 10,000 to 1 in 20,000 anesthetic procedures. (Mertes et al., 2011).

Remimazolam, an ultrashort-acting benzodiazepine, has recently become available for general anesthesia and procedural sedation. Previous studies have suggested that remimazolam may cause less intraoperative hypotension than propofol, possibly because it provides greater hemodynamic stability during induction of anesthesia. (Liu et al., 2021; Choi et al., 2024). As the use of remimazolam continues to increase, it has been suggested as a potential but under-recognized trigger of perioperative hypersensitivity reactions. Among the various causative agents, neuromuscular blocking agents are the most frequently implicated triggers, with rocuronium being one of the commonly reported agents. In addition, newly introduced anesthetic agents, such as remimazolam, have limited data regarding their potential to induce hypersensitivity reactions, making clinical decision-making more complex in cases of suspected drug-induced anaphylaxis.

Patients with a prior history of perioperative anaphylaxis represent a high-risk population, and re-exposure to anesthetic agents poses a significant clinical dilemma. The lack of definitive identification of the causative agent, potential cross-reactivity, and urgency of surgical intervention further complicate anesthetic planning. Therefore, strategies to minimize the risk of recurrence-including avoidance of suspected triggers and the use of preoperative prophylactic medications-are of considerable clinical importance.

In this report, we describe a case of successful re-anesthesia in a patient who previously experienced anaphylactic shock following induction with remimazolam and administration of rocuronium, highlighting the potential role of preoperative prophylaxis in preventing recurrence.

Case Presentation

A 77-year-old female with underlying hypertension and hyperlipidemia presented for elective laparoscopic cholecystectomy. The patient had a known history of drug allergies to nonsteroidal anti-inflammatory drugs (NSAIDs) and acetaminophen.

Premedication was administered 30 minutes prior to surgery and included intramuscular glycopyrrolate (0.2 mg), intramuscular midazolam (1 mg), and intravenous famotidine (20 mg). Upon arrival in the operating room, the initial vital signs were as follows: blood pressure 200/90 mmHg, heart rate 60 beats/min, and oxygen saturation (SpO2) 99%.

Anesthesia was induced with remimazolam (20 mg) and rocuronium (50 mg). Two minutes after induction, the patient developed profound hypotension with a blood pressure of 52/40 mmHg, heart rate of 87 beats/min, and SpO2 of 98%. Peak inspiratory pressure (PIP) increased to 27 cmH2O, and end-tidal CO2 (EtCO2) decreased to 25 mmHg.

Phenylephrine (200 mcg) was administered immediately after the drop in blood pressure; however, no significant improvement was observed. An additional 300 mcg of phenylephrine was subsequently administered, but blood pressure remained unresponsive. Epinephrine (1:10,000) was then administered in escalating doses of 10 mcg, 20 mcg, 30 mcg, 40 mcg, and 50 mcg. Following epinephrine administration, blood pressure transiently increased and PIP decreased to below 20 cmH2O. However, as the effect of epinephrine diminished, hypotension and elevated PIP recurred, requiring repeated administration.

Despite these events, the surgery proceeded as planned. After the operation, the patient was hemodynamically stable in the post-anesthesia care unit and was transferred to the intensive care unit (ICU). In the ICU, oxygen was administered via nasal cannula at 2 L/min, maintaining SpO2 above 95%. The patient was subsequently transferred to the general ward after stabilization.

Based on the clinical presentation of severe hypotension and an increase in peak inspiratory pressure (PIP) to 27 cmH2O, the patient described in this case report was classified as having Grade III severity according to the Ring and Messmer

four-step (I-IV) grading scale. Prompt administration of epinephrine prevented progression to a more critical state.

An anaphylactic reaction was suspected, and laboratory evaluation revealed an elevated histamine level of 2.89 (normal < 1.23) and a mildly elevated tryptase level of 12.1.

Five months later, the patient was readmitted for emergency surgery due to an incisional hernia. General anesthesia was again induced using the same doses of remimazolam and rocuronium, in accordance with the previously applied anesthetic protocol. However, on this occasion, preoperative prophylaxis with methylprednisolone (Methysol, 50 mg) and pheniramine (4 mg) was administered prior to induction. No signs of hypersensitivity or anaphylactic reaction were observed, and the anesthesia course was uneventful.

DISCUSSION

Identification of the causative agent in perioperative anaphylaxis remains challenging. Although skin prick and intradermal tests are widely used, their sensitivity is limited and false-negative results have been reported. Emerging agents such as remimazolam may lack standardized testing protocols, further complicating diagnosis. In addition, serum biomarkers including tryptase and histamine may not always be obtained promptly, limiting diagnostic accuracy. Consequently, definitive identification of the offending agent is often not possible, and clinical judgment remains essential.

Assessment of serum tryptase and histamine levels soon after symptom onset can aid in the diagnosis of perioperative anaphylaxis, although normal laboratory findings cannot definitively rule it out. (Dewachter & Savic, 2019). Perioperative anaphylaxis commonly presents with a rapid onset and is often characterized by acute cardiovascular instability, including severe hypotension, tachycardia, bradycardia, or arrhythmias occurring near cardiac arrest. (Uusalo & Kuuskoski, 2026). Confirming the diagnosis of perioperative anaphylaxis remains challenging because both in vivo and in vitro diagnostic methods can produce false-negative results, especially for newly introduced drugs without validated testing protocols. (Orihara et al., 2020; Mertes & Tacquard, 2023; Takazawa et al., 2021). Therefore, definitive identification of the causative agent is often not feasible in routine clinical practice, and diagnosis relies on temporal correlation, clinical manifestations, and indirect evidence.

In this case, no formal allergy testing was performed, precluding definitive identification of the causative agent and limiting diagnostic certainty. Therefore, causal inference was based on indirect clinical and institutional evidence. During an 18-month period at our institution, hypersensitivity reactions were observed in 4 of 2,415 patients receiving remimazolam with rocuronium, whereas no cases were identified among 3,665 patients receiving propofol with rocuronium. Although this difference did not reach statistical significance (Fisher's exact test, p approximately 0.08), the exclusive occurrence of reactions in the remimazolam group suggests a potential association. However, interpretation of this finding is limited by the retrospective nature of the observation, the small number of events, and the presence of confounding factors, particularly the difference in age distribution between groups. Therefore, these results should be considered hypothesis-generating, and further studies with controlled designs are warranted to clarify the potential role of remimazolam in perioperative hypersensitivity reactions. Evidence for optimal re-anesthesia in patients with prior perioperative anaphylaxis remains limited and is largely based on case reports and expert opinion. Standard strategies include avoidance of suspected agents, alternative drug selection, and preoperative antihistamine and corticosteroid prophylaxis; however, their efficacy is not fully established. Therefore, individualized risk assessment and close intraoperative monitoring are essential.

Hypersensitivity reactions to NSAIDs, especially those mediated through COX-1 inhibition, are generally considered pharmacologic class effects and are not known to exhibit immunologic cross-reactivity with neuromuscular blocking agents or intravenous anesthetic agents. However, such patients may exhibit a broader predisposition to perioperative hypersensitivity, suggesting an underlying susceptibility rather than specific cross-reactivity. This case adds to the limited evidence and may support consideration of structured, risk-stratified anesthetic planning in patients with prior severe perioperative anaphylaxis.

Premedication with corticosteroids and antihistamines is commonly used in high-risk patients to reduce mast cell mediator release and reaction severity. However, it does not reliably prevent IgE-mediated reactions. In this case, the absence of recurrence after prophylaxis may also reflect variability in patient response, and a direct protective effect cannot be confirmed.

Despite these limitations, this case suggests that safe re-exposure to previously implicated anesthetic agents may be feasible under carefully structured perioperative management, including vigilant monitoring and adjunctive prophylactic strategies, and adds to the limited evidence supporting a risk-stratified approach in patients with prior severe perioperative anaphylaxis.

This case may provide clinically relevant insight in situations where re-exposure to essential anesthetic agents is unavoidable despite prior suspected hypersensitivity reactions.

CONCLUSION

This case suggests that safe re-exposure to previously implicated anesthetic agents may be possible in selected high-risk patients when re-exposure is unavoidable and structured perioperative planning, preoperative prophylaxis, and vigilant intraoperative monitoring are applied. However, the absence of recurrence in this single case does not confirm a definitive protective effect of prophylaxis, and further studies are required to establish optimal preventive strategies.

REFERENCES

1. Hepner, D. L., & Castells, M. C. (2003). Anaphylaxis during the perioperative period. Anesthesia & Analgesia, 97(5), 1381-1395. https://doi.org/10.1213/01.ANE.0000082993.84883.7D
2. Mertes, P. M., Malinovsky, J. M., Jouffroy, L., Aberer, W., Terreehorst, I., Brockow, K., et al. (2011). Reducing the risk of anaphylaxis during anesthesia: 2011 updated guidelines for clinical practice. Journal of Investigational Allergology and Clinical Immunology, 21(6), 442-453.
3. Liu, T., Lai, T., Chen, J., Lu, Y., He, F., Chen, Y., & Xie, Y. (2021). Effect of remimazolam induction on hemodynamics in patients undergoing valve replacement surgery: A randomized, double-blind, controlled trial. Pharmacology Research & Perspectives, 9(5), e00851. https://doi.org/10.1002/prp2.851
4. Choi, S. H., Min, K. T., Park, E. K., & Park, S. (2024). Comparison of hypotension incidence between remimazolam and propofol in patients with hypertension undergoing neurosurgery: Prospective, randomized, single-blind trial. BMC Anesthesiology, 24, 198. https://doi.org/10.1186/s12871-024-02578-7
5. Dewachter, P., & Savic, L. (2019). Perioperative anaphylaxis: Pathophysiology, clinical presentation and management. BJA Education, 19(10), 313-320. https://doi.org/10.1016/j.bjae.2019.06.002
6. Uusalo, P., & Kuuskoski, R. (2026). Anaphylaxis and perioperative drug reactions. British Journal of Surgery, 113(1), znaf287. https://doi.org/10.1093/bjs/znaf287
7. Orihara, M., Takazawa, T., Nagumo, K., Sakamoto, S., Horiuchi, T., & Saito, S. (2020). Interpreting the results of early skin tests after perioperative anaphylaxis requires special attention: A case report and review of literature. Journal of Anesthesia, 34(4), 624-629. https://doi.org/10.1007/s00540-020-02802-x
8. Mertes, P. M., & Tacquard, C. (2023). Perioperative anaphylaxis: When the allergological work-up goes negative. Current Opinion in Allergy and Clinical Immunology, 23(4), 287-293. https://doi.org/10.1097/ACI.0000000000000912
9. Takazawa, T., Yamaura, K., Hara, T., Yorozu, T., Mitsuhata, H., Morimatsu, H., et al. (2021). Practical guidelines for the response to perioperative anaphylaxis. Journal of Anesthesia, 35(6), 778-793. https://doi.org/10.1007/s00540-021-03005-8