



CARDIAC ARREST FOLLOWING REMIMAZOLAM INDUCED ANAPHYLAXIS AFTER INDUCTION OF GENERAL ANESTHESIA : A CASE REPORT

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ABSTRACT

Remimazolam besylate, a newly developed drug, is linked to various anaphylaxis cases. We report a case of a 72-year-old man who experienced a cardiac arrest due to severe anaphylaxis immediately after general anesthesia induction. Although remimazolam is structurally similar to midazolam, the patient was not allergic to midazolam as demonstrated before and after anaphylaxis. This report highlights the potential risk of allergic reactions to remimazolam.

KEYWORDS : dextran40; general anesthesia induction; midazolam; remimazolam; anaphylaxis

INTRODUCTION

Remimazolam is an ultrashort-acting benzodiazepine that has been used to induce general anesthesia in Korea since August 2020, in advance of the rest of the world. Remimazolam was synthesized by introducing a carboxylic ester side group into midazolam, and its chemical structure is similar to that of midazolam (Figure 1). Compared to other benzodiazepines, remimazolam has a faster onset and less accumulation after prolonged infusion due to its shorter duration of action. In addition, remimazolam is less likely to cause hypotension than propofol and has been shown to be effective and safe for general anesthesia induction in high-risk surgical patients. Recently, several case reports of anaphylaxis caused by remimazolam have been published. However, its clinical characteristics are not fully understood, especially in terms of cross-reactivity to other benzodiazepines.

The aim of this report is to describe a case of remimazolam anaphylaxis in a patient who was not allergic to midazolam and to review the literature on remimazolam anaphylaxis. All applicable guidelines were followed, and written consent for publication of the case report was obtained from the patient.

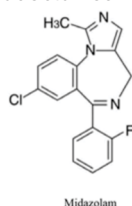
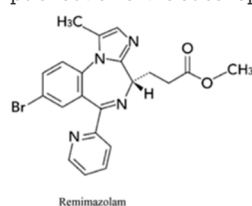


Figure 1. Chemical structures of the remimazolam and midazolam.

Case Description

A 72-year-old man scheduled for laparoscopic-assisted cholecystectomy was administered remimazolam for the induction of general anesthesia. His medical history included hyperlipidemia, and reflux esophagitis. Before the surgery, the patient had undergone multiple upper and lower endoscopic procedures, during which midazolam and propofol were administered without any adverse reactions. Before anesthetic induction, the patient's vital signs were as follows: blood pressure, 169/104 mmHg; heart rate, 73 bpm; and SpO₂, 98% (room air). Anesthesia was induced with intravenous remifentanyl 0.26 mcg/kg/min, and remimazolam 10mg. Rocuronium 50 mg was administered, and he was intubated with a video laryngoscope. Tracheal intubation was successfully performed. After intubation, low end-expiratory CO₂, high airway pressure and concurrent circulatory collapse were observed. At around 14:05, endotracheal intubation was performed. At approximately 14:11, blood

pressure was measured at 85/55 mmHg, and phenylephrine 100 mcg was administered repeatedly, but the blood pressure did not increase. At 14:13, blood pressure dropped to 55/35 mmHg, and QRS widening and ST elevation were observed on the ECG. At 14:14, epinephrine 1 mg was administered, but no pulse was detected, so chest compressions were started. After administering another epinephrine 1 mg at 14:17, polymorphic ventricular tachycardia (VT) was noted on ECG at 14:18. While preparing for defibrillation, the rhythm converted to sinus rhythm and ROSC was achieved. The patient was subsequently awakened from anesthesia, extubated, and the surgery was canceled. The patient was then transferred to the ICU. On ICU admission, the airway compliance improved, and the next day, tracheal edema was attenuated and the patient was extubated. Blood tests showed normal tryptase levels but elevated plasma Histamine level. The patient recovered well, and it was planned to perform laparoscopic cholecystectomy under general anesthesia again one week later. Anesthesia was induced with intravenous remifentanyl 0.26 mcg/kg/min, and propofol 80mg. Rocuronium 30 mg was administered, and he was intubated with a video laryngoscope. There were no specific events during the surgery, and the total duration of general anesthesia was 54 minutes. The patient recovered well and was discharged two days later. Remifentanyl, rocuronium and remimazolam were used just before anaphylaxis. Latex and antibiotics were not used. Remifentanyl and rocuronium had been used without anaphylactic reactions in other situations, such as endoscopy. Based on the above findings, we determined that the allergen was remimazolam, and intradermal testing was not performed.

DISCUSSION

Remimazolam besylate is a new benzodiazepine sedative characterized by its ultra-short duration of action. Remimazolam and midazolam have similar chemical structures (Figure 1) and clinical characteristics. Both induce mild cardiovascular depression and their anesthetic effects are antagonized by flumazenil. Perioperative benzodiazepine-induced anaphylaxis is extremely rare. Remimazolam-associated anaphylaxis is predicted to be rare as well. However, this is not an established fact owing to the lack of widespread use. Diagnosing perioperative anaphylaxis can be challenging due to the variety of drugs used, including anesthetics, antibiotics, neuromuscular blockers, and latex. Recently, cases of remimazolam-induced anaphylaxis have been consistently reported. Further investigation revealed that dextran 40, which is an excipient contained in the remimazolam solution and is frequently

associated with anaphylaxis.

CONCLUSIONS

Remimazolam should not be ruled out as the causative drug if anaphylaxis occurs during anesthesia induction. During the allergy test, dextran 40 should also be evaluated and provocation testing for remimazolam should be initiated at a low dose under careful monitoring of the patient's vital signs. We believe that this case report and literature review will support the establishment of a mechanism for remimazolam anaphylaxis and allergy testing protocols in the future.

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