

Remimazolam for Procedural Sedation During Cardioversion

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Abstract

Background: Remimazolam is a benzodiazepine with sedative, anxiolytic, and amnestic properties similar to those of midazolam. However, its elimination is novel as it undergoes metabolism by tissue esterases with a half-life of 5 - 10 min and a limited context-sensitive half-life, thereby resulting in a rapid dissolution of its clinical effects. Initial clinical work has demonstrated its efficacy for the induction of general anesthesia, as an adjunct to maintenance anesthesia, and for procedural sedation.

Methods: We retrospectively reviewed our experience with the use of remimazolam for sedation during cardioversion in adult patients.

Results: The study cohort included six patients, ranging in age from 22 to 68 years. Intravenous remimazolam was the primary agent for all procedures. All six patients received a single bolus dose of remimazolam while two patients received a continuous infusion after the bolus dose. Two patients received adjunctive agents (fentanyl 100 µg). No clinically significant respiratory or hemodynamic adverse effects were noted in any patient. Adequate amnesia was achieved as none of the six patients recalled the cardioversion.

Conclusion: Our preliminary experience demonstrates that remimazolam may be an effective agent for sedation during cardioversion without significant impact on hemodynamic or respiratory function. In adult patients, a single 5 mg bolus dose of remimazolam provided effective amnesia and sedation for the procedure.

Keywords: Remimazolam; Cardioversion; Procedural sedation; Benzodiazepine

Introduction

Remimazolam is an ester metabolized derivative of the in-

travenous (IV) benzodiazepine, midazolam [1-3]. Food and Drug Administration (FDA) approval for its use in adults was granted in 2020. Like midazolam, remimazolam acts on the gamma-aminobutyric acid (GABA-A) receptor producing amnestic, sedative, and anxiolytic effects. However, what makes it unique is that remimazolam undergoes a novel metabolic pathway of hydrolysis by tissue esterase. Preliminary clinical experience has demonstrated that remimazolam is an effective agent for procedural sedation or as an adjunct to general anesthesia in the adult population [4, 5].

Patients undergoing cardioversion generally require procedural sedation to provide amnesia and anxiolysis. Traditionally, agents such as propofol or midazolam are the primary agents used in this clinical scenario. We present our preliminary experience with the use of remimazolam as the primary agent for procedural sedation in adults during cardioversion. Potential advantages of remimazolam are discussed and dosing strategies presented.

Materials and Methods

This retrospective review was approved by the Institutional Review Board of Nationwide Children's Hospital (Columbus, Ohio). This study was conducted in compliance with the ethical standards of Nationwide Children's Hospital for research involving human subjects as well as with the Helsinki Declaration. As a retrospective study, the need for individual written informed consent was waived.

From a larger database of patients receiving remimazolam for sedation, patients were identified who received remimazolam for sedation during cardioversion. Demographic data obtained included age, weight, comorbid conditions, and gender. Remimazolam dosing information included the dose, dosing changes during the procedure, mode of administration (bolus or continuous infusion), and duration of infusion. If additional adjunctive agents were administered, the agent and the dose were identified. Intraoperative and postoperative adverse effects including hypotension, bradycardia, respiratory arrest, apnea, or hypoventilation were identified. According to our usual clinical practice, the following guidelines were used to identify adverse hemodynamic or respiratory effects: bradycardia ≤ 50 beats/min; hypotension - systolic blood pressure (SBP) less than 90 mm Hg; respiratory insufficiency - apnea, respiratory rate less than 8 breaths/min or end-tidal carbon dioxide (ETCO₂) more than 50 mm Hg. Additionally, the use of rescue medications including anticholinergic or vasoactive agents (epinephrine, phenylephrine, vasopressin,

Manuscript submitted April 24, 2025, accepted May 31, 2025
Published online June 16, 2025

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doi: <https://doi.org/10.14740/cr2080>

Table 1. Clinical Patient Data and Remimazolam Dosing

Patient number	Demographics (age, weight, height, gender)	Remimazolam dosing	Adjunctive agents	Outcomes and follow-up
1	51-year-old, 70.2 kg, 175 cm, man	3.51 mg bolus followed by a continuous infusion at 10 - 20 µg/kg/min duration preparation and performance of the procedure.	Fentanyl 100 µg	Successful cardioversion. Recovery time of 62 min. Discharged home the same day.
2	22-year-old, 63.9 kg, 174 cm, man	5 mg bolus followed by a continuous infusion at 10 - 20 µg/kg/min duration preparation and performance of the procedure.	Fentanyl 100 µg	Successful cardioversion. Recovery time of 65 min. Reported nausea and pain. Received ondansetron and acetaminophen. Discharged home the same day.
3	68-year-old, 81.8 kg, 177 cm, man	5 mg bolus	None	Successful cardioversion. Recovery time of 54 min. Discharged home the same day, expired at home 3 months later.
4	49-year-old, 81.6 kg, 178 cm, man	5 mg bolus	None	Successful cardioversion. Recovery time of 43 min. Remained inpatient for dofetilide initiation. Discharged home 4 days later.
5	42-year-old, 66.3 kg, 172 cm, man	5 mg bolus	None	Successful cardioversion. Recovery time of 20 min. Discharged home the next day.
6	34-year-old, 150.4 kg, 179 cm, man	5 mg bolus	None	Successful cardioversion. Recovery time of 30 min. Remained inpatient for initiation of sotalol therapy.

or ephedrine) or the need for bag-valve-mask ventilation was noted.

Results

The study cohort included six patients who required procedural sedation from April 2022 through September 2024. The patients ranged in age from 22 to 68 years (median age 46.5 years) and in weight from 63.9 to 150.4 kg (Table 1). In all six patients, the procedure involved was synchronized cardioversion for conversion of stable atrial flutter or atrial fibrillation. Given the relative elective nature of the procedure, all the patients were *nil per os* for at least 6 h. Routine monitoring and care during procedural sedation followed the standards set by the American Society of Anesthesiologists [6]. The conduct of sedation and patient monitoring were supervised by an attending anesthesiologist.

IV remimazolam was the primary agent for all procedures. For clinical use, remimazolam was reconstituted in normal saline from a lyophilized powder using the vial size provided by the manufacturer to achieve a final concentration of 20 mg/8 mL (2.5 mg/mL). The medication was provided in a syringe and administered by an infusion pump during intraoperative care. Based on our routine clinical practice for continuous IV infusions, administration was calculated in µg/kg/min and not mg/kg/h.

All six patients received a single bolus dose of remimazolam. In addition, two patients received a continuous infusion after the bolus dose. The first patient of the cohort received a single bolus dose of 3.51 mg while the remaining five patients received a single bolus dose of 5 mg. In addition to the bolus dose, the first two patients also received a continuous infusion

at 10 - 20 µg/kg/min during preparation and performance of the procedure. Patients 1 and 2 of the cohort were the only patients who received adjunctive agents. Both patients received fentanyl (100 µg) in addition to the remimazolam. No other sedative or analgesic agents were administered for the remaining patients in the cohort. The infusions in both patients were started immediately after the bolus dose was given. No clinically significant respiratory or hemodynamic adverse effects were noted in any of the patients in our cohort. For all six of the procedures, a native airway was maintained during sedation and the procedure, with supplemental oxygen provided via a nasal cannula at 2 L/min. None of the patients required the administration of a vasoactive agent, an anticholinergic agent or fluid to treat hemodynamic changes. Adequate amnesia was achieved as none of the six patients had any recall of the cardioversion. No patient required conversion to general anesthesia and all six cardioversions were successful with conversation to normal sinus rhythm with one cardioversion.

Discussion

Our preliminary experience demonstrates the successful use of remimazolam for sedation and the provision of amnesia during cardioversion. Given the general brevity of the procedure, we opted to use a single bolus dose (5 mg) in the final four patients as the continuous infusion was not deemed necessary. However, supplemental bolus doses may need to be considered if a second attempt at cardioversion is required. As has been demonstrated in previous clinical trials, remimazolam provided adequate sedation without clinically significant effects on respiratory or hemodynamic function. All patients maintained a native airway and spontaneous ventilation during the proce-

ture. There were no significant adverse hemodynamic effects. Various prospective trials comparing general anesthesia with remimazolam versus propofol have shown improved hemodynamic stability, less hypotension, and a decreased need for vasoactive agents [7-9].

During cardioversion, there are a wide variety of practice models and agents that have been used alone or in combination to achieve the goal of sedation, anxiolysis, and amnesia [10-12]. A key concern when choosing an agent in this scenario includes its potential impact on respiratory, hemodynamic, and electrophysiological properties, especially in patients with congenital or acquired heart defects. As the majority of cardioversions are performed with a native airway, a limited impact on respiratory function and upper airway patency is preferable when selecting a primary agent. Given the brevity of the procedure, a rapidly acting agent whose effects dissipate rapidly is also beneficial. Perhaps most importantly, given the potential for associated comorbid cardiac diseases or depressed cardiac output with supraventricular tachyarrhythmias, hemodynamic stability is also required.

Other investigators have evaluated the safety of remimazolam for the induction and maintenance of anesthesia in adults with associated end-organ cardiac involvement and comorbid diseases including American Society of Anesthesiologists physical class 3 patients, patients presenting for cardiac surgery, during catheterization suite ablation of atrial fibrillation, and in patients with aortic stenosis [13-18]. Additionally, preliminary data have demonstrated a lack of effect on cardiac conduction [19, 20].

Given the retrospective nature of the manuscript, certain limitations must be recognized including the lack of controlled dosing regimens with two patients getting an infusion after the bolus dose. Our data must be considered preliminary as both efficacy and adverse effects may be difficult to ascertain from a case series with only six patients. As data were extracted from the electronic medical record, it is not feasible to accurately outline onset and recovery times. Subjective criteria were used to measure the extent and efficacy of anesthesia (patient response to the cardioversion and questioning of patient recall). Objective criteria such as depth of anesthesia monitoring were not used. In the best effort to identify adverse effects, we looked for clinical interventions that may have been required to treat adverse effects such as the administration of a vasoactive or anticholinergic agent or the need for bag-valve-mask ventilation rather than rigorous criteria. Furthermore, without a specific comparator group using another agent, the potential superiority of remimazolam over other more commonly used agents cannot be shown.

In summary, remimazolam with its rapid onset and prompt dissolution of its clinical effects following its metabolism by tissue esterase may be an effective agent for procedural sedation during cardioversion. Clinical studies have demonstrated limited effects on hemodynamics and respiratory function. Remimazolam has been shown to be effective for procedural sedation in a wide variety of clinical scenarios for both invasive and non-invasive procedures including sedation during fiberoptic intubation, cardiac catheterization, radiologic imaging, and gastrointestinal endoscopic procedures [3, 19, 21]. Our preliminary clinical experience demonstrates that a single

5 mg bolus dose of remimazolam provides adequate amnesia and sedation during cardioversion when a single shock is required. If a second shock is necessary, a supplemental dose (2.5 mg) may be required to ensure amnesia.

Acknowledgments

None to declare.

Financial Disclosure

None to declare.

Conflict of Interest

None to declare.

Informed Consent

Followed the guidelines of the IRB of Nationwide Children's Hospital (Columbus, Ohio). Informed consent was obtained for hospital/anesthetic care and the use of de-identified information for publication.

Author Contributions

Preparation of initial, subsequent, and final drafts: MH and CK; direct patient care, review and approval of final document: MC and CM; concept, writing, and review of all drafts: JDT.

Data Availability

Any inquiries regarding supporting data availability of this study should be directed to the corresponding author.

Abbreviations

FDA: Food and Drug Administration; GABA: gamma aminobutyric acid; IV: intravenous

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