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Case Report

Anesthetic management using remimazolam in a patient with atrial flutter: a case report

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Abstract: Remimazolam is a new intravenously administered ultra-short-acting benzodiazepine used in anesthesia or sedation. Remimazolam offers several advantages over other short-acting sedatives, including an organ-independent metabolism and rapid and predictable onset and recovery. Furthermore, remimazolam shows less cardiovascular-inhibitory effects than other anesthetics. Atrial flutter is a form of cardiac arrhythmia that is associated with serious health-related outcomes and a substantial economic burden. Acute onset of atrial flutter can cause cardiac dysfunction, hypotension, and myocardial ischemia. Moreover, patients with atrial flutter are likely to have an increased risk of both atrial fibrillation and stroke. In this case report, a patient with a 1-year history of atrial flutter underwent general anesthesia for robot-assisted laparoscopic prostatectomy. Using continuous remimazolam infusion, anesthesia and surgery were successfully completed without sudden changes in the patient's blood pressure, heart rate, or electrocardiogram. This case report describes the first reported use of remimazolam to induce general anesthesia in a patient with atrial flutter. The findings suggest that remimazolam can reduce the hemodynamic risk during anesthesia in patients with arrhythmias such as atrial flutter, and is a suitable option for anesthesia in patients with arrhythmias.

Keywords: Remimazolam, atrial flutter, anesthesia, intravenous, midazolam, propofol

Introduction

The different methods of inducing and maintaining general anesthesia include inhalation, and intravenous administration, each of which has unique characteristics. The method of anesthesia is determined on the basis of the patient's age, sex, underlying disease, and procedure type. Among the existing methods, intravenous anesthesia does not cause an excitatory phase during induction [1, 2]. Remimazolam is a new ultra-short-acting intravenously administered benzodiazepine for anesthesia or sedation that shows a simulated context-sensitive half-life of 6.8 ± 2.4 min after a 4-h infusion [3].

Atrial flutter was first recorded on an electrocardiogram (ECG) by Einthoven in 1906 [4]. Atrial fibrillation and atrial flutter are cardiac arrhythmias associated with serious health-related outcomes and substantial economic burden [5]. Although the risk of stroke caused by atrial flutter is still unclear, Gula et al. [5] reported that patients with isolated atrial flutter had a greater risk of atrial fibrillation and stroke than the general population. In patients with cardiac arrhythmia, hemodynamic changes or sudden changes in heart rate (HR) during anesthesia can be life-threatening. Therefore, when inducing anesthesia in patients with an arrhythmia such as atrial flutter, various factors, including cardiac function, must be considered.

The patient in this case study had a malignant neoplasm of the prostate and elected to undergo a robot-assisted laparoscopic prostatectomy (RALP). He had undergone an aortic valve replacement 6 years previously and had normal ECG findings since then. However, atrial flutter was observed approximately 1 year prior to prostate surgery, and the patient was prescribed anticoagulant therapy to prevent an arrhythmia-induced stroke. Because the patient had atrial flutter, hemodynamic instability caused by factors such as an uncontrolled HR

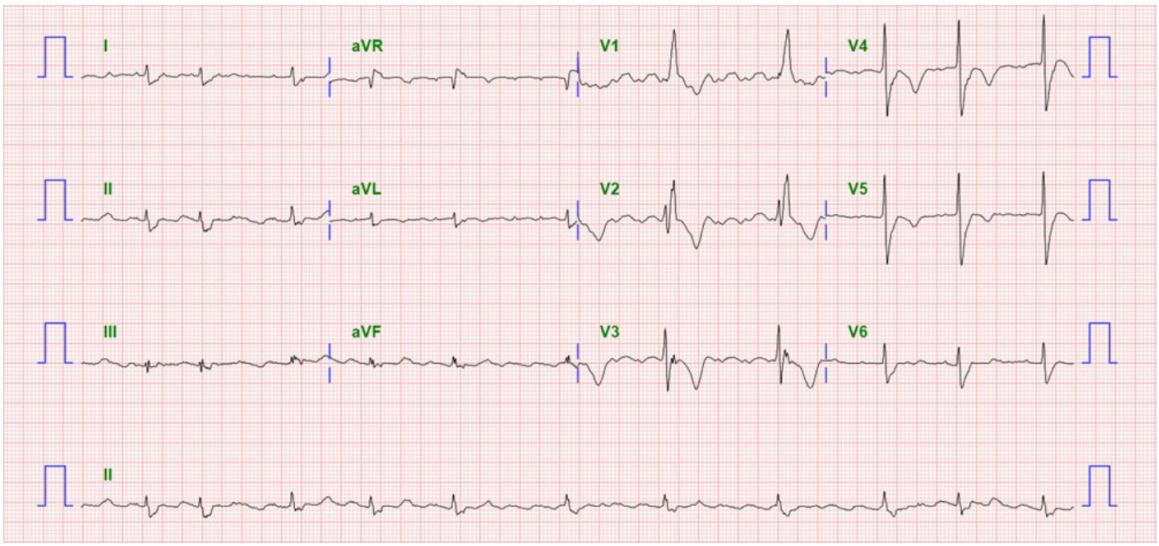

Figure 1. Preoperative electrocardiogram showing the atrial flutter, variable atrioventricular block, right bundle branch block, and lateral ischemia.

or decreased blood pressure (BP) could result in the transition from atrial flutter to atrial fibrillation [6]. Therefore, remimazolam, which has relatively few cardiovascular-depressant effects [7], was used to induce general anesthesia. The use of remimazolam during anesthesia has been reported previously [8-12]. However, only a few reports have described continuous anesthesia using remimazolam in patients with arrhythmia. To the best of our knowledge, this is the first case report describing induction of general anesthesia using remimazolam in a patient with atrial flutter.

Case report

This case report was approved by the Chungbuk National University Hospital Clinical Research Review Committee (approval number 2022-01-019-001). The patient provided informed consent for its publication.

A 68-year-old man (height, 171 cm; weight, 81 kg) was scheduled to undergo a RALP for a malignant neoplasm of the prostate. The patient had undergone an aortic valve replacement for severe aortic stenosis 6 years previously and was followed up in the cardiology department. There were no abnormal ECG findings after heart surgery. However, atrial flutter was diagnosed 1 year prior to the RALP, and anticoagulant therapy was prescribed.

Our preoperative ECG evaluation identified atrial flutter with a variable atrioventricular block, right bundle branch block, and lateral ischemia (**Figure 1**). Preoperatively, the patient reported no symptoms, such as palpitations. The ECG and BP were monitored in the operating room, and a left radial arterial line was placed under ultrasonographic guidance to monitor hemodynamic parameters. The ECG indicated a rhythm of atrial flutter. The HR and BP were 56-60 beats/min and 137/94 mmHg, respectively, prior to the induction of anesthesia. The bispectral index (BIS) was monitored to assess sedation during surgery.

Remimazolam (6 mg/kg/h) was administered to induce anesthesia and no occurrence of pain at the injection site or other adverse symptoms were noted. The HR was maintained at 60-65 beats/min, and the BP was 124/68 mmHg. As the patient lost consciousness, a remifentanil infusion at 0.3 μg/kg/min was initiated, followed by intravenous rocuronium (50 mg); glycopyrrolate was not administered. After intubation, the HR and BP increased to 75 beats/min and 165/100 mmHg, respectively, and subsequently decreased to 55-60 beats/min and 104/69 mmHg, respectively, after 10 min. Thereafter, no sudden changes in HR, BP, or ECG findings were observed during surgery (**Figure 2**); Remifentanil was infused at 0.1-0.15 μg/kg/min and remimazolam was administered at 1 mg/kg/h to maintain sedation under BIS monitoring.

The total operative time was 310 min, and muscle relaxation was reversed using sugam-

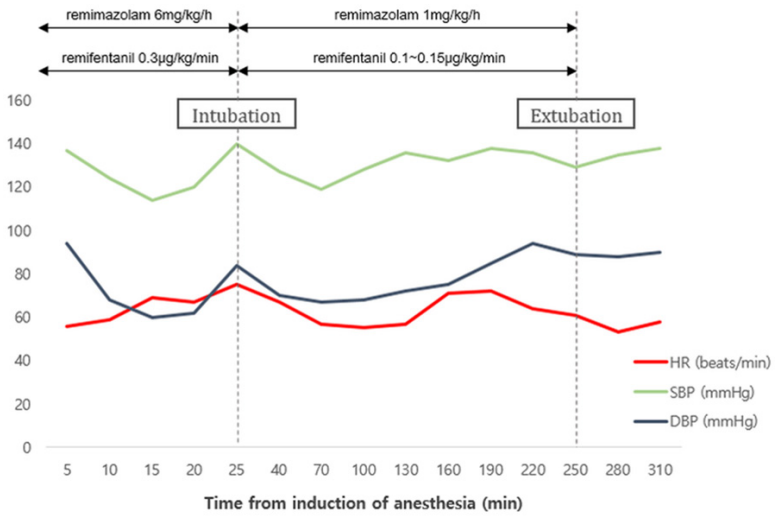

Figure 2. Blood pressure and heart rate changes during surgery.

madex (Bridion, Merck & Co., Inc., Kenilworth, NJ, USA). Postoperative HR and BP were 70-75 beats/min and 151/96 mmHg, respectively. No changes were observed in the postoperative ECG.

The patient was transferred to the general recovery room and observed for 30 min by ECG and BP monitoring. The ECG revealed no changes. HR and BP were maintained at approximately 60 beats/min and 135/80 mmHg, respectively. The patient was conscious and able to communicate without difficulty. No abnormal symptoms, such as chest pain or palpitations were observed. The patient was then transferred to the hospital ward.

On postoperative day 1, ECG indicated the presence of atrial flutter with variable atrioventricular block, right bundle branch block, and lateral ischemia (**Figure 3**). Observation by a cardiologist revealed no significant changes in cardiac function. On postoperative day 7, the patient was discharged and scheduled for follow-up assessments at the cardiology and urology departments.

Discussion

Atrial flutter is caused by macro-re-entry between the free wall of the right atrium and the atrial septum containing the cavotricuspid isthmus located between the tricuspid annulus and inferior vena cava [13]. Atrial flutter differs from atrial fibrillation, which is caused by a giant regression path and multiple regression wave fronts [14, 15].

Few studies have investigated the epidemiology of atrial flutter in the general population, and the overall incidence of atrial flutter adjusted for the U.S. population is 88 per 100,000 [16]. The prevalence of atrial flutter has been reported to be 1.25% in men, 0.59% in women, and 0.88% in the general population [16]. The incidence of atrial flutter increases with age [16].

The acute onset of atrial flutter can impair cardiac function, reduce BP, and cause myocardial ischemia. Permanent atrial flutter with rapid ventricular beating can lead to tachycardia-mediated cardiomyopathy [13]. High-risk factors for atrial flutter include male sex, older age, and the presence of underlying heart failure or chronic obstructive pulmonary disease [16].

Song et al. [6] reported a case in which atrial flutter was observed immediately after general anesthesia induction; atrial flutter converted to atrial fibrillation and necessitated postponement of surgery. This shows that atrial arrhythmia is likely to occur during anesthesia induction. In addition, Amar [17] reported that preoperative heart rate, preoperative sympathetic dominance, autonomic dysfunction, and inflammatory changes in the atrial myocardium were risk factors in patients aged ≥ 60 years; these factors may be possible mechanisms of atrial arrhythmias in this patient demographic.

Acute atrial flutter can be treated using drugs or electrical cardioversion, depending on the patient's hemodynamic stability [13]. The drug acts by decreasing the duration of the circulatory wave front by prolonging the refractory period in the tachycardia circuit without slowing conduction; generally this is achieved by administering class III antiarrhythmics such as ibutilide, dofetilide, azimilide, and sotalol [13]. Class I drugs (flecainide, procainamide, quinidine), class III drugs, and amiodarone are used to prevent the recurrence of atrial flutter, and

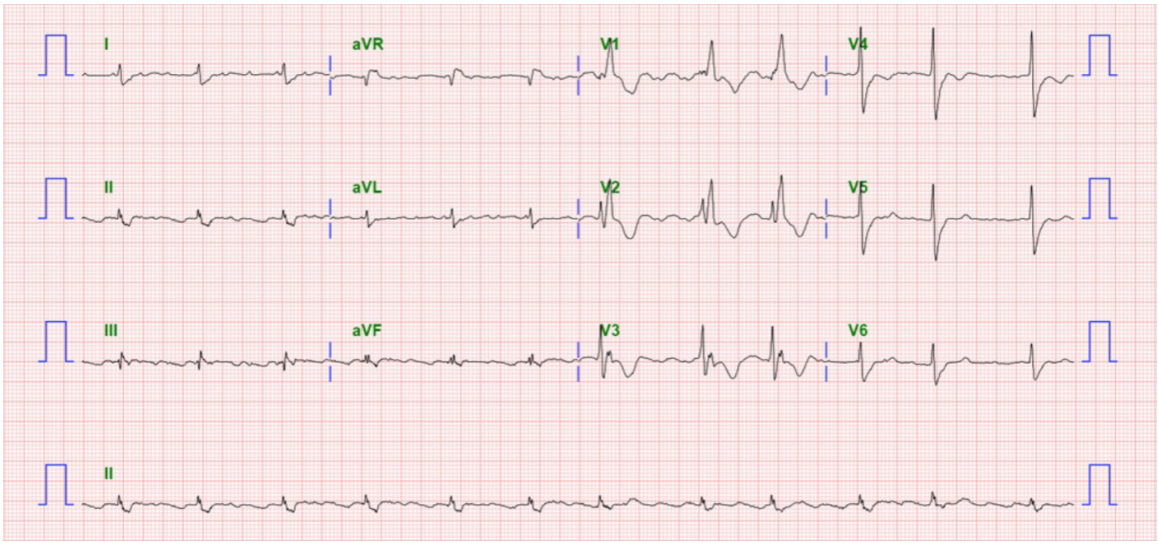

Figure 3. On postoperative day 1, electrocardiogram showing the atrial flutter, variable atrioventricular block, right bundle branch block, and lateral ischemia.

external electrical cardioversion has also been used for atrial flutter termination [13].

Several methods can be used to induce anesthesia. Among these, intravenous anesthetics are generally used for induction and maintenance of general anesthesia because they elicit no excitatory phase during induction, cause less nausea and vomiting after surgery, are associated with no risks of pollution, and are relatively simple to administer [1, 2]. The most frequently used intravenous anesthetic is propofol, which has a rapid onset time and allows quick cognitive recovery. However, propofol has several disadvantages, including cardiovascular depression, injection-related pain, metabolic acidosis, and propofol infusion syndrome [2]. In addition, the use of lipid formulations of propofol can predispose patients to bacterial infections.

Midazolam, a benzodiazepine sedative, has been used to induce anesthesia. However, its long half-life and resultant accumulation over the course of continuous administration may cause arousal delays [18]. Thus, midazolam is not used for maintenance of anesthesia [18]. However, remimazolam, a midazolam derivative that functions as an ultra-short-acting benzodiazepine agonist with high binding affinity to the γ-aminobutyric acid (GABA) receptor, can be used to maintain anesthesia [3]. Because of its organ-independent metabolism as well as rapid and predictable onset and recovery, remimazolam offers potential advantages over other fast-acting sedatives such as midazolam and propofol [19-21]. Moreover, remimazolam has a similar sedation effect profile as midazolam, and multiple-dose studies have reported remimazolam-induced sedation and rapid reversibility that were adequate for colonoscopies [22]. Moreover, remimazolam does not cause pain when administered. Although the general use of flumazenil is not recommended due to the possible need for re-sedation, it may be used in emergencies to reverse sedation [23].

Doi et al. [7] reported that remimazolam could be safely and effectively used in surgery for patients with ASA class III. In their study, remimazolam did not cause a dose-dependent decrease in BP, and both 6 mg/kg/h and 12 mg/kg/h doses were considered equally safe for hemodynamic stability. Similarly, Saito et al. [8] reported a case in which the patient was anesthetized using remimazolam during cardiopulmonary bypass for cardiac surgery.

The patient in this report had previously undergone heart surgery and showed no major complications subsequently. He developed atrial flutter a year prior to RALP and was prescribed anticoagulation therapy. The history of atrial flutter was one of the factors to consider during anesthesia and surgery, since an increase in HR or sudden changes in BP during anesthesia induction or surgery may have affected the patient's hemodynamic stability. Thus, caution

was required to avoid the possibility of atrial flutter progressing to ventricular fibrillation. The administration of propofol may have resulted in an increased HR and a decreased BP due to its cardiovascular-depressant effects. Therefore, remimazolam, which has lower cardiovascular-depressant effects than propofol, was used in anesthesia induction and maintenance. Glycopyrrolate was not administered because of its potential to inhibit vagus nerve stimulation. No sudden changes in HR or BP were observed during anesthesia maintenance with remimazolam, except immediately after intubation and after waking the patient. BIS monitoring showed that the patient was in a sleeping state without abnormalities until the end of the surgery. Sugammadex was used at the end of anesthesia to quickly reverse muscle relaxation and avoid the use of glycopyrrolate, which is generally used at the end of anesthesia.

In summary, remimazolam is an ultra-short-acting benzodiazepine-class drug that can be used to overcome the limitations of midazolam for maintaining anesthesia. As highlighted in this case report, remimazolam can induce, and maintain, hemodynamically stable anesthesia in patients with arrhythmia; therefore, it can be a safe alternative to the conventionally used propofol. Additional studies and larger datasets are needed to corroborate these findings and to develop guidelines for the clinical use of remimazolam in patients with arrhythmia or heart disease.

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