INTRODUCTION

Remimazolam, a benzodiazepine newly approved in January 2021 in Korea, is ultra-short acting, which compensates for the onset and recovery time limitations of midazolam. Remimazolam is rapidly hydrolyzed by tissue esterases to an inactive carboxylic acid metabolite and has a high clearance and small volume of distribution. Similar to the characteristics of other benzodiazepines, flumazenil can be administered to reverse the sedative effect of remimazolam. In addition, compared to propofol, remimazolam is associated with no pain on injection, less hemodynamic depression, and superior efficacy as a sedative for general anesthesia. As outpatient procedures with monitored anesthesia care become more popular in terms of medical costs, recovery time, and patient satisfaction, we expected that remimazolam is preferable in ambulatory surgery owing to its rapid onset, short elimination half-life, fast recovery, and reversal agent availability. Currently, studies on monitored anesthesia care with remimazolam are scarce; therefore, we present four cases in which ambulatory surgery was performed under remimazolam sedation.

1.1 | Case descriptions

1.1.1 | Patient 1

This patient was a 31-year-old woman (height, 162cm; weight, 51 kg) who was diagnosed with cervical intraepithelial neoplasia grade II based on punch biopsy results. The patient had no underlying diseases except for polycystic ovary syndrome, which did not require medication. She was scheduled for loop electrosurgical excision (LEEP) under monitored anesthesia care in an ambulatory setting. A preoperative anesthetic evaluation was completed before the procedure. Considering her sensitivity to pain, we used intravenous remimazolam as a sedative after the patient provided informed consent.

On the day of surgery, an intravenous catheter was placed and maintained with normal saline. Standard and...
bispectral index (BIS) monitoring were applied in the operating room, and her initial vital signs were as follows: blood pressure (BP), 129/83 mmHg; heart rate (HR), 72 beats/min; respiratory rate (RR), 22 breaths/min; and oxygen saturation (SpO₂), 100%; the BIS was 92. Vital signs were monitored continuously, and BP was measured approximately every 5 min and additionally as needed. Remimazolam infusion was administered at 6 mg/kg/h until loss of consciousness (LoC, defined as modified observer assessment of alertness/sedation [MOAA/S] score ≤2) was established. The patient’s alertness gradually decreased; the MOAA/S score decreased to 2, and the BIS was 61 at 1 min 40 s after induction. Following the LoC, a maintenance dose was administered at 1 mg/kg/h. The patient’s vital signs at that time were as follows: BP, 113/72; HR, 70 beats/min; RR, 18 breaths/min; and SpO₂ 100%. The patient was placed in the lithotomy position and draped. At 5 min after induction, 50 μg of fentanyl was administered; the procedure commenced at 9 min after induction. A facial grimace was observed at the start of the excision; 25 μg of fentanyl was further administered, and analgesia was well maintained thereafter. The procedure was completed in 3 min, and remimazolam infusion was discontinued at that time. In total, 25.1 mg of remimazolam was administered during the procedure. The MOAA/S score was maintained below 2 until the end of the procedure and the BIS did not exceed 70. The patient’s vital signs were stable without major changes, and there were no adverse events including injection pain, bradycardia, hypotension, and respiratory depression. At 5 min after discontinuation of remimazolam, the patient opened her eyes in response to her name, and the BIS increased to 77. At 7 min after discontinuation of remimazolam, she was fully awake and able to move all extremities voluntarily. Her vital signs remained stable, and no postoperative adverse events were reported in the recovery room. The patient was completely amnestic throughout the procedure. As the discharge criteria were quickly met, she was discharged from the recovery room on the same day and reported a satisfying experience.

1.1.2 | Patient 2

Patient 2 was a 45-year-old woman (height, 167 cm; weight, 41 kg) who was scheduled for resectoscopic polypectomy to remove endometrial polyps. The patient had no underlying diseases. A preoperative anesthetic evaluation was completed followed by provision of informed consent. Her initial vital signs were as follows: BP, 112/65 mmHg; HR, 90 beats/min; RR, 17 breaths/min; and SpO₂ 100%. The BIS was 97, and the vital signs were monitored in the same manner as the previous case. Remimazolam infusion was administered at 6 mg/kg/h, and LoC was established at 2 min after induction. The BIS was 78 at this time. Similar to Patient 1, remimazolam infusion was maintained at 1 mg/kg/h and fentanyl 40 μg was administered 4 minu before the start of the operation. A facial grimace was observed at the start of cervical dilatation; therefore, 25 μg of fentanyl was further administered. The procedure was completed in 23 min, and remimazolam infusion was discontinued at that time. In total, 36.1 mg of remimazolam was administered during the procedure. Meanwhile, LoC was maintained without adjustment of the remimazolam dose, and no further administrations of fentanyl were required. The BIS did not exceed 80. At 4 min after discontinuation of remimazolam, the patient opened her eyes in response to her name, and the BIS increased to 80. Perioperative vital signs were within normal limits, and no adverse events were reported.

1.1.3 | Patient 3

Patient 3 was a healthy 49-year-old woman (height, 153 cm; weight, 53 kg) who was scheduled for hysteroscopic dilatation, curettage, and biopsy for endometrial hyperplasia. A preoperative anesthetic evaluation was completed, and informed consent was provided. Her initial vital signs were as follows: BP, 106/84 mmHg; HR, 66 beats/min; RR, 13 breaths/min; and SpO₂ 100%; the BIS was 91, and vital signs were monitored in the same manner as the previous cases. Remimazolam infusion was administered at 6 mg/kg/h, and LoC was established at 1 min 50 seconds; the BIS was 58. Following the LoC, a maintenance dose was administered at 1 mg/kg/h. The patient’s vital signs at that time were as follows: BP, 111/55 mmHg; HR, 72 beats/min; RR, 15 breaths/min; and SpO₂ 100%. Fifty μg of fentanyl was administered, and the procedure commenced at 4 min after induction. Analgesia was well maintained, and additional fentanyl administration was not required. The procedure was completed in 5 min, and remimazolam infusion was discontinued at that time. In total, 21.3 mg of remimazolam was administered during the procedure. LoC was maintained until the end of the procedure, and the BIS did not exceed 67. The patient’s vital signs were stable without major changes, and there were no adverse events. At 4 min after discontinuation of remimazolam, the patient opened her eyes and the BIS increased to 75. At 9 min after discontinuation of remimazolam, she was fully awake and able to move all extremities voluntarily.

1.1.4 | Patient 4

Patient 4 was a healthy 40-year-old woman (height, 165 cm; weight, 55 kg) who was scheduled for LEEP to
evaluate a cervical intraepithelial neoplasia. A preoperative anesthetic evaluation was completed, and informed consent was provided. Her initial vital signs were as follows: BP, 117/95 mmHg; HR, 75 beats/min; RR, 14 breaths/min; and SpO₂ 100%; the BIS was 98, and vital signs were monitored in the same manner as the previous cases. Similar to the previous cases, remimazolam was intravenously administered at 6 mg/kg/h and LoC was established at 1 min 24 s; the BIS was 80. Following the LoC, a maintenance dose was administered at 1 mg/kg/h. The patient’s vital signs at that time were as follows: BP, 114/81 mmHg; HR, 69 beats/min; RR, 13 breaths/min; and SpO₂ 100%. Fifty μg of fentanyl was administered, and the procedure commenced at 4 min after induction. A facial grimace and body movements were observed at the start of the excision; therefore, 25 μg of fentanyl was further administered. The procedure was completed in 6 min, and remimazolam infusion was discontinued at that time. In total, 22.2 mg of remimazolam was administered during the procedure. Until the end of the procedure, LoC was maintained, and the BIS did not exceed 68. The patient’s vital signs were within normal limits, and there were no adverse events. At 12 min after discontinuation of remimazolam, the MOAA/S score was still 2 and the BIS was 65. Thus, we administered 0.5 mg of flumazenil (Flunil, Bukwang Pharmaceutical Co., Ltd), the patient opened her eyes, and the BIS increased to 81 in 1 min. At 14 min after discontinuation of remimazolam, she was fully awake and able to move all extremities voluntarily. Thereafter, the patient did not return to a sedated state again. The overall timeline graph including vital parameters of four patients is represented in Figure 1.

2 | DISCUSSION

In these four cases, we successfully provided monitored anesthesia care with intravenous remimazolam for LEEP, resectoscopy, and hysteroscopy. Moreover, the patients did not report any injection or serious perioperative pain owing to the administration of small doses of fentanyl. Furthermore, adverse events including bradycardia, hypotension, and respiratory depression were not observed. These results suggest that remimazolam administered with fentanyl can provide sufficient monitored anesthesia care for simple gynecological day surgeries.

According to a previous randomized phase IIb/III trial in 2019,² patients were administered 6 or 12 mg/kg/h remimazolam for induction and 1 mg/kg/h for maintenance of anesthesia. Both regimens were superior to a standard dose of propofol with regard to general anesthesia efficacy. In this trial, time to LoC was longer in the 6 mg/kg/h group compared with the 12 mg/kg/h group (102.0 and 88.7 s, respectively), although the dose required to achieve LoC was less in the 6 mg/kg/h group than that in the 12 mg/kg/h group (0.17 and 0.29 mg/kg). The time to the patients opening their eyes after the discontinuation of remimazolam was 14.9 min in the 6 mg/kg/h group.

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**FIGURE 1** Timeline graph including vital parameters. LoC—loss of consciousness; BP—blood pressure; HR—heart rate; RR—respiratory rate; SpO₂—oxygen saturation; MOAA/S—modified observer assessment of alertness/sedation score; BIS—bispectral index
and 14.5 min in the 12 mg/kg/h group. Considering the short surgery time of our cases, we administered remimazolam at 6 mg/kg/h for induction to reduce the total dose of remimazolam. The times to LoC in our cases were 100, 120, 110, and 84 s in Patients 1, 2, 3, and 4, respectively, and the doses to achieve LoC were 0.17, 0.2, 0.18, and 0.14 mg/kg, respectively. These results are consistent with those of the previous trial. However, the times to eye opening after discontinuation of remimazolam in our cases were 5, 4, 9, and 13 minutes, respectively, which are significantly shorter compared with those of the previous trial. Although these results may be due to short exposure to the drug and administration of flumazenil, the fast recovery and availability of a reversal agent are favorable factors in ambulatory surgery. In a previous case report in which remimazolam was used as a sedative, re-sedation was reported even though flumazenil was administered. Our patient who received flumazenil did not report re-sedation; however, she was instructed to remain in the day-surgery ward for 2 h.

In another prospective randomized controlled trial, remimazolam with target-controlled intravenous remifentanil provided effective and safe sedation for hysteroscopy. Although the BIS was not recorded in the previous study, remimazolam provided effective sedation based on the MOAA/S score and fewer reported adverse events, including injection pain (only reported in 1 patient of 41). According to our cases, remimazolam offered sufficient sedation for various gynecological day surgeries based on both the MOAA/S and BIS scores. Because BIS values in remimazolam sedation indicated an adequate depth of sedation similar to propofol, our results are consistent with those of the previous study. Complaints of pain on injection were not reported.

In the above studies, remifentanil was administered for analgesia using a target-controlled infusion; however, we also administered fentanyl. In a previous study, 1 μg/kg of fentanyl 4 min before the start of the surgery had similar effects on recovery time, discharge time, and satisfaction scores compared to 0.05 μg/kg/min of remifentanil in monitored anesthesia care with propofol. Although an additional 25 μg dose of fentanyl was administered in three of our cases, 1 μg/kg of fentanyl 4 min before the start of the procedure can provide effective analgesia and patient satisfaction.

Currently, the cost of remimazolam does not provide an economic advantage over propofol due to its generic availability, which may limit its usefulness and cost-effectiveness in certain circumstances. Nevertheless, remimazolam seems to be a favorable alternative to propofol for patients who are very sensitive to pain or nervous about anesthesia because it does not cause injection pain and has an available reversal agent. Furthermore, although further clinical trials are needed, remimazolam may be considered the sedative of choice in patients who are expected to be hemodynamically unstable.

Remimazolam was recently studied on bolus administration and can be used as an induction agent without dose adjustments in patients with renal and hepatic impairment, gradually expanding its clinical application. Although further studies are needed, this case report suggests another potential field of application of remimazolam with its short duration and availability of immediate antagonism.

**AUTHOR CONTRIBUTIONS**
So Ron Choi designed this case report. Tae Hyung Kim wrote the manuscript. Deuk Won Eom coauthored the manuscript and searched literature. Ji Wook Jung coauthored the manuscript. Sang Yoong Park provided medical consultation and reviewed the manuscript.

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**CONFLICTS OF INTERESTS**
The authors declare that there are no conflicts of interest regarding the publication of this paper.

**DATA AVAILABILITY STATEMENT**
The data that support the findings of this study are available from the corresponding author upon reasonable request.

**CONSENT**
Written informed consent was obtained from the patients for publication of the case details and any accompanying images.

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**REFERENCES**
1. Pambianco DJ, Borkett KM, Riff DS, et al. A phase IIb study comparing the safety and efficacy of remimazolam and midazolam in patients undergoing colonoscopy. *Gastrointest Endosc*. 2016;83(5):984-992.
2. Doi M, Morita K, Takeda J, Sakamoto A, Yamakage M, Suzuki T. Efficacy and safety of remimazolam versus propofol for general anesthesia: a multicenter, single-blind, randomized, parallel-group, phase IIb/III trial. *J Anesth*. 2020;34(4):543-553.
3. Worthington MT, Antonik LJ, Goldwater DR, et al. A phase I, dose-finding study of multiple doses of remimazolam (cns 7056) in volunteers undergoing colonoscopy. *Anesth Analg*. 2013;117(5):1093-1100.

4. Centini G, Troia L, Lazzeri L, Petraglia F, Luisi S. Modern operative hysteroscopy. *Minerva Ginecol*. 2016;68(2):126-132.

5. Yamamoto T, Kurabe M, Kamiya Y. A mechanism of re-sedation caused by remimazolam. *J Anesth*. 2021;35(3):467-468.

6. Zhang X, Li S, Liu J. Efficacy and safety of remimazolam besylate versus propofol during hysteroscopy: single-Centre randomized controlled trial. *BMC Anesthesiol*. 2021;21(1):1-8.

7. Doi M, Hirata N, Suzuki T, Morisaki H, Morimatsu H, Sakamoto A. Safety and efficacy of remimazolam in induction and maintenance of general anesthesia in high-risk surgical patients (ASA class III): results of a multicenter, randomized, double-blind, parallel-group comparative trial. *J Anesth*. 2020;34(4):491-501.

8. Ryu JH, Kim JH, Park KS, Do SH. Remifentanil-propofol versus fentanyl-propofol for monitored anesthesia care during hysteroscopy. *J Clin Anesth*. 2008;20(5):328-332.

9. Chae D, Kim H-C, Song Y, Choi YS, Han DW. Pharmacodynamic analysis of intravenous bolus remimazolam for loss of consciousness in patients undergoing general anaesthesia: a randomised, prospective, double-blind study. *Br J Anaesth*. 2022;129(1):49-57.

10. Stöhr T, Colin PJ, Ossig J, et al. Pharmacokinetic properties of remimazolam in subjects with hepatic or renal impairment. *Br J Anaesth*. 2021;127(3):415-423.

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