

# Asleep Flexible Bronchoscopic Intubation with Remimazolam Sedation for Difficult Airway Management: A Case Series

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## ABSTRACT

Flexible Bronchoscopic Intubation (FBI) is the accepted standard for managing difficult airways. Sedation is frequently used during awake intubation to make the procedure tolerable. However, this technique has complications, including respiratory depression, hypoxemia, aspiration and airway trauma. Asleep FBI is an alternative approach. Remimazolam, an ultra-short-acting benzodiazepine, is emerging as a suitable drug for FBI of deeply sedated patients with spontaneous breathing. It has several desirable qualities, including rapid onset and offset, easily titratable sedation levels, anxiolysis and hemodynamic stability. We present three successful cases of asleep FBI for patients with difficult airways using Remimazolam as the primary sedative.

**Keywords:** Remimazolam; Sedation; Flexible bronchoscopic intubation; Benzodiazepine

## INTRODUCTION

Flexible Bronchoscopic Intubation (FBI) is critical for difficult airway procedures. Several reports have described various topicalization methods and sedation techniques to secure the airways [1]. However, the choice of technique depends on the clinical circumstances and feasibility of keeping the patient awake or asleep. Awake FBI (also known as awake Fiberoptic Intubation) is facilitated by the administration of sedatives. It is often recommended by experts, but awake techniques require complex psychomotor skills, flowless topicalization of the upper airway and regular practice [2]. Rosentock et al., reported first attempt successful intubation rate of 79% by experienced anesthesiologists (investigators) [3]. Fifteen percent of patients who underwent awake FBI with mild sedation reported discomfort, including feelings of suffocation and coughing [4]. Over sedation leading to loss of spontaneous ventilation is a common complication of this technique [5].

Asleep FBI, while maintaining spontaneous ventilation, may circumvent several issues and improve patient experience. The commonly used midazolam/fentanyl combination is associated with disinhibition, respiratory depression and hypoxemia [6]. Dexmedetomidine does not cause respiratory depression but is long-acting and irreversible. Based on the experience of one of

the authors, dexmedetomidine is not easily titratable and it takes 15-20 min to achieve the desired level of sedation [7].

Remimazolam is a recently introduced ultra-short-acting benzodiazepine with a rapid onset and offset of action and is associated with minimal respiratory depression. The reversibility of the drug and its weight-independent clearance add to its safety in cases of overdose. This study aimed to test the suitability of remimazolam for asleep FBI and document its cardiovascular and respiratory effects.

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## CASE PRESENTATION

We present three patients who received Remimazolam as the primary sedative for FBI.

### Case 1

The patient was a 75-year-old male with a medical history of diabetes mellitus, hypertension, coronary artery disease and a right partial rhinectomy for recurrent nasal squamous cell carcinoma. Physical examination revealed an extensive right upper lip defect in the nasal cavity and palate and a mallampation

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class IV airway with limited mouth opening. Preoperatively, the patient was administered 5 ml of 4% nebulized lidocaine. After placement of standard monitors, remimazolam 6 mg was administered, followed by two additional doses (2 mg/injection) to achieve a Modified Observer's Assessment of Alertness/Sedation (MOAA/S) score of 2 ("responds only after mild prodding or shaking"). The superior laryngeal nerves were anesthetized by placing 4% lidocaine-soaked pledgets in the pyriformis fossae using satinsky forceps. The patient did not respond to oropharyngeal manipulation. The junior resident inserted the Fiberoptic Intubation (FB) over the airway and passed it through the cords on his first attempt. Throughout the procedure, the patient breathed spontaneously (RR 16-19). His SpO<sub>2</sub> was 96-100% and his Blood Pressure (BP) was close to the baseline.

### Case 2

The patient was a 73-year-old male with a history of diabetes mellitus, benign prostatic hyperplasia and multiple bilateral knee surgeries. He presented with neck pain following a vehicle collision. Computed Tomography (CT) of the cervical spine revealed a Hangman's fracture, type III odontoid fracture, C1-C4 epidural hematoma and C3-C6 spinal canal stenosis. Physical examination revealed a limited range of motion of the neck secondary to traumatic injury. Preoperatively, the patient was treated with 5 ml of 4% nebulized lidocaine. Supplemental O<sub>2</sub> was administered via a nasal cannula. Remimazolam 10 mg (5 mg × 2) was also administered and cetacaine was simultaneously sprayed on the patient's oropharynx. The patient was sedated and 4% lidocaine-soaked pledgets were placed on the tonsillar pillars. While the patient was still breathing spontaneously (MOAA/s=2), an ovassapian oral airway was inserted. The trainee's first attempt was unsuccessful because of excessive secretions. An attending anesthesiologist visualized the vocal cords and inserted a 7.5 mm Endotracheal Tube (ETT). The patient breathed spontaneously (RR 10-13) throughout the procedure with a SpO<sub>2</sub> of 97-100%.

### Case 3

The patient was a 50-year-old male with a history of hypertension and substance abuse. He presented with symptoms of central cord syndrome and C3-C4 cord edema after a vehicle collision. Neck stability was maintained using a C-spine collar. The patient tested positive for phencyclidine, making him uncooperative during physical examination. He had a Mallampati class III airway and weakness in the right and left upper extremities. The patient was scheduled for posterior cervical decompression and fusion. Preoperatively, the patient was treated with glycopyrrolate 0.4 mg to reduce secretion. In the OR, monitors were applied and supplemental O<sub>2</sub> was provided by a nasal cannula. Remimazolam 18 mg was administered in four doses (8, 4, 4 and 2 mg). Once MOAA/S was achieved and the patient was adequately pre-oxygenated (SpO<sub>2</sub>, 100%), 4% lidocaine-soaked pledgets were placed in the pyriformis fossae. The senior resident introduced the scope into the oropharynx using a 9.0 mm ovassapian intubating airway. Once the epiglottis and cords were visualized, 10 cc of 2% lidocaine was sprayed directly into the vocal cords. The bronchoscope was passed atraumatically through the vocal cords and a 7.5 mm ETT was advanced and secured. The patient breathed spontaneously (RR 14-16) throughout the procedure with SpO<sub>2</sub> of 98-100%.

## RESULTS AND DISCUSSION

This report describes the FBI of asleep but spontaneously breathing patients sedated with Remimazolam as the primary sedative. The advantages of asleep FBI include patient comfort resulting in better intubating conditions, improved quality of oropharynx anesthesia, cardiovascular stability, minimal risk of laryngospasm, easy manipulation of the scope and, as a result, shorter intubation time. It can be performed when awake intubation is intolerable or impossible for the patient. Heidegger et al. reported successful FBI within one minute in 60% (394, out of 657) of asleep patients *versus* zero in awake (0, out of 955)[8]. Pandit et al., found that FBI was successful on the first attempt in 28 of 30 (93%) asleep patients; the two remaining patients required two attempts [9].

Asleep FBI requires careful titration with sedatives that can be easily reversed. Our experience suggests that Remimazolam, a recently introduced ultra-short-acting benzodiazepine, is a good alternative for asleep FBI [10]. The esterase linkage in Remimazolam permits rapid hydrolysis that contributes to the unique and favorable pharmacological profile of the drug, including rapid onset and offset of action, predictable duration of action and minimal tissue accumulation. Thus, Remimazolam offers precise control of drug effects via the titration of boluses and rapid recovery when discontinued. In case of oversedation, this agent can be reversed by Flumazenil.

The efficacy of Remimazolam for procedural sedation has been demonstrated in several studies [11-13]. Compared with placebo and midazolam for moderate sedation during bronchoscopy, Remimazolam was more efficacious for overall procedural success, had a faster onset of sedation and shorter recovery times. The incidence of adverse effects (hypotension, hypertension, ECG changes and hypoxia) was similar to or lower than that of the midazolam or placebo group. A post hoc analysis of this trial investigated the effect of sedation level on vital signs and adverse effects [13]. The authors concluded that patients with older and higher American Society of Anesthesiologists (ASA) physical status spent more time in deeper sedation, but there was no difference in vital signs.

Based on the results of registration trials, the Remimazolam package insert recommends the administration of a 5 mg dose over 1 min followed by 2.5 mg supplemental doses in 2 min intervals for patients with ASA 1-2 (lower doses for ASA 3-4). The investigators aimed to achieve a MOAA/S level of 3 (response only after name is called loudly and/or repeatedly). Considering the safety profile of Remimazolam (minimal respiratory and cardiovascular depression), we administered significantly higher doses to achieve a MOAA/S of 2. For example, Patient 3 required 18 mg of Remimazolam administered over 5 min to achieve the desired sedation level.

The patient breathed spontaneously and the O<sub>2</sub> saturation remained above 96% throughout the procedure. Chen, et al. compared Remimazolam and Propofol for efficacy and safety in patients who underwent colonoscopy and upper endoscopy [14]. The authors reported that patients in the Remimazolam group had a decreased incidence of respiratory depression, desaturation, pain upon injection, increased bilirubin levels, hypotension and shorter recovery time than those in the Propofol group. Our data suggest minimal respiratory and cardiovascular variations in patients undergoing FBI under sedation, corresponding to an MOAA/S of 2 (Table 1).

Case	Initial BP, mmHg	Blood pressure before ETT insertion, mmHg	Initial heart rate (bpm)	Heart rate after ETT insertion (bpm)	Time to MOAA/S of 2, min	Total dose of Remimazolam, mg	Lowest O <sub>2</sub> before securing the airway	Time to intubation after achieving MOAA/s of 2
1	159/86	144/84	83	79	5	10	96	1
2	162/102	150/90	99	90	4	10	97	2
3	171/98	148/89	72	80	7	18	98	1

**Note:** ETT: Endotracheal Tube; MOAA/S: Modified Observer's Assessment of Alertness/Sedation.

**Table 1:** Clinical data of the cases.

## CONCLUSION

Our case report documented successful asleep FBI using Remimazolam, an ultra-short-acting Benzodiazepine, in three patients with anticipated difficult airways. Remimazolam provides adequate sedation in terms of patient satisfaction and optimal intubation conditions. It effectively induces anxiolysis while maintaining spontaneous ventilation and cardiovascular instability. Its rapid onset, offset, ease of titration and reversibility make it a good sedative for asleep FBI. Studies comparing Remimazolam with well-established alternatives, particularly Dexmedetomidine, are encouraged. These will validate the usefulness of Remimazolam in managing difficult airways.

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