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CASE REPORT

Combination of Remimazolam and Remifentanil for Procedural Sedation and Analgesia in a Patient with Morbid Obesity Undergoing Gastrointestinal Endoscopy under Continuous Positive Airway Pressure: A Case Report

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Sedation in patients with morbid obesity undergoing gastrointestinal endoscopy (GIE) frequently causes respiratory depression. Remimazolam, a gamma-aminobutyric acid receptor agonist, is safer than propofol as it has fewer cardiovascular and respiratory adverse effects. We report a case of successful GIE under sedation and analgesia with a combination of remimazolam and remifentanil, respectively, in a patient with morbid obesity experiencing obstructive sleep apnea (OSA). Remimazolam ensured safe sedation, preventing complications such as respiratory depression and hypotension. Dose adjustment of remifentanil can minimize its adverse effects. Therefore, the combination of remimazolam and remifentanil is a promising choice for performing GIE in patients with morbid obesity and OSA.

Key words: Morbid obesity, remimazolam, remifentanil, gastrointestinal endoscopy, obstructive sleep apnea, continuous positive airway pressure

INTRODUCTION

Intravenous anesthesia with propofol and opioids without the need for intubation is preferred by anesthesiologists for short surgical or diagnostic procedures. However, hypotension, respiratory depression, and airway obstruction resulting in hypoxemia or hypoxia during procedural sedation and analgesia (PSA) during gastrointestinal endoscopy (GIE) are common, particularly in patients with morbid obesity.[1] Remimazolam, a novel short-acting Gamma-aminobutyric acid$_A$ receptor agonist, promotes rapid recovery from PSA and is associated with less severe circulatory and respiratory depression than propofol. Prior research demonstrates that the effects of remimazolam on the cardiovascular and respiratory systems are relatively minimal.[2] We present the case of a patient with morbid obesity who underwent GIE under sedation and analgesia with remimazolam and remifentanil, respectively.

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CASE REPORT

A 42-year-old woman (height of 153.5 cm; weight of 105.3 kg; body mass index of 44.69 kg/m^2; adjusted body weight [ABW] of 70 kg) was scheduled for GIE. She had a history of severe obstructive sleep apnea (OSA), and was treated with a continuous positive airway pressure (CPAP) machine. Laboratory examination results were within normal limits. Electrocardiography before surgery showed a normal sinus rhythm. Before the examination, standard monitors were prescribed, and she was placed in the left lateral decubitus position. A CPAP machine was used during the procedure [Figure 1]. End-tidal carbon dioxide (EtCO2) levels were tracked using capnometry, with a catheter positioned beneath the CPAP mask. The EtCO2 waveform consistently demonstrated that the airway was unobstructed

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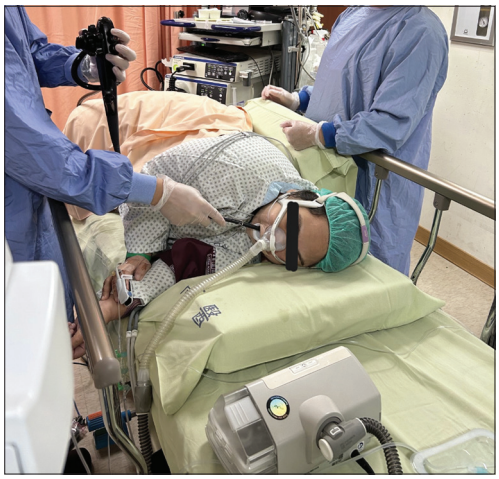

Figure 1: The application of continuous positive airway pressure during gastrointestinal endoscopy in the patient

[Supplementary Figure 1]. In addition, chest wall movement was vigilantly monitored by a skilled nurse anesthetist. Remimazolam was diluted with 20 mL of normal saline to a concentration of 1 mg/mL. An initial dose of 7 mg remimazolam was administered (dosing based on ABW, 0.1 mg/kg). The continuous remimazolam pump was then maintained at 0.2 mg/kg/h (dosing based on ABW), and a target-controlled infusion of remifentanil at an effect-site concentration (Ce) of 2.0 ng/mL (dosing based on ABW) was initiated based on the Minto model to maintain an observer assessment of alertness/sedation scale score between 3 and 4.[3] The gastroscope was inserted after the Ce of remifentanil reached 4.0 ng/mL, ensuring the patient remained under light sedation. In response to the patient's coughing, our approach involved titrating remifentanil to alleviate stimulation rather than adjusting remimazolam. If respiratory issues emerged due to elevated remifentanil concentration, we promptly titrated the remifentanil dose to address potential apnea, although apnea was not observed in this case. After the gastroscopic examination, the Ce of remifentanil was adjusted to 1.0 ng/mL, and colonoscopy was performed uneventfully. The entire procedure was completed in 22 min. The cumulative doses of remimazolam and remifentanil were 12.1 mg and 153 mcg, respectively. In addition, stable hemodynamics and respiratory immobility were maintained throughout the procedure. After regaining consciousness, the patient reported no recollection of pain during the procedure and expressed extreme satisfaction.

DISCUSSION

To our knowledge, this is the first case of the successful use of the combination of remimazolam and remifentanil for PSA during GIE in a morbidly obese patient receiving CPAP therapy for severe OSA.

Midazolam and propofol, with or without opioids, have been most used for PSA in GIE. Borkett *et al*. reported comparing various remimazolam concentrations with midazolam for procedural sedation of patients undergoing upper GIE. Remimazolam, administered at concentrations of 0.10–0.20 mg/kg, induces rapid sedation with an acceptable safety profile. Unlike midazolam, which typically induces sedation within 5 min, remimazolam induces sedation within 1.5–2.5 min; moreover, the successful rate of the procedure in the remimazolam groups was reportedly higher than those in the midazolam group.[4] Although propofol yields rapid sedation onset and recovery, its adverse effects, such as respiratory depression and hypotension, pose challenges during procedures. A phase III clinical trial showed noninferiority of remimazolam to propofol in inducing successful sedation for upper GIE. Compared to propofol, remimazolam not only yielded faster recovery but also substantially decreased the incidences of treatment-related hypotension, respiratory depression, and overall adverse events.[2] Moreover, a separate study including elderly patients demonstrated significant advantages of remimazolam over propofol, including significantly less incidences of hypotension, bradycardia, respiratory depression, and injection-site pain.[5] We had anticipated the emergence time with remimazolam to be similar to that with propofol based on previous findings. For instance, Koyama *et al*. reported the use of remimazolam and remifentanil to prevent delayed emergence and postoperative respiratory insufficiency in a patient without neuromuscular blocking agents.[6] A study comparing remimazolam and propofol showed significantly faster emergence times with remimazolam than with propofol (compliance with verbal commands in 5 min with remimazolam vs. 14 min with propofol). However, re-sedation was observed in 22% of remimazolam-treated patients in this study.[7]

The safety profile of sedative agents, particularly when combined with analgesics, is critical in PSA. In a simulation study of common propofol and propofol-opioid dosing regimens for upper endoscopy, propofol alone mostly led to inadequate conditions for esophageal instrumentation, and the addition of remifentanil or fentanyl improved esophageal instrumentation conditions with a similar recovery time.[8] Previous studies have reported adverse effects of propofol use, such as apnea, hypoxemia, hypotension, and bradycardia.[1] In our case, we effectively avoided hypoxemia and hypotension by gradually increasing the dose of remifentanil from 2.0 to 4.0 ng/mL to suppress the gag reflex. Our outcome differed from those reported by Motamed *et al*.,[9] who found that remifentanil concentrations between 3 and 5 ng/mL caused bradypnea in 40% of patients and hypoxemia in 6% of patients. This is likely owing to the coadministration of remimazolam in our case, whereas no other sedative was administered in this study.

Nonetheless, awareness of the potential risks of the combined use of remifentanil and remimazolam is critical to patient safety. A case report on intravenous anesthesia with remifentanil and remimazolam reported severe laryngospasm in the patient.[10] During the administration of remifentanil, the patient experienced loss of consciousness and acute desaturation, consistent with laryngospasm. Rapid injection of remifentanil is highly likely the cause of this adverse reaction. As exemplified in our case, a gradual and circumspect approach to dosage adjustments may mitigate such adverse events and contribute to safer PSA practices.

The use of remimazolam in combination with short-acting opioids such as remifentanil in high-risk patients such as morbid obesity, elderly, and hepatic and renal failure patients remains relatively unexplored. Further prospective research or randomized trials with larger sample sizes are needed to determine the efficacy and safety of this combination.

CONCLUSION

The combination of remimazolam and remifentanil provided adequate analgesia and sedation depth without respiratory depression or hypotension in our patient with morbid obesity and severe OSA treated with CPAP.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient has given her consent for her image and other clinical information to be reported in the journal. The patient understands that her name and initials will not be published and due efforts will be made to conceal her identity, but anonymity cannot be guaranteed.

Data availability statement

The data that support the findings of this study are available from the corresponding author, ZF Wu, upon reasonable request.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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Supplementary Figure 1: The screenshot of the monitor