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Etomidate versus Remimazolam in Elderly Patients Undergoing Painless Gastroenteroscopy

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Abstract: *Objective:* To compare the hemodynamic stability of etomidate and remimazolam during painless gastroscopy and evaluate the safety of remimazolam in elderly patients undergoing gastroscopy. *Methods:* A total of 100 elderly patients aged 65–80 years, with American Society of Anesthesiologists (ASA) physical status I–II, who underwent painless gastrointestinal endoscopy were included in this study. The patients were randomly assigned to receive either 0.2 mg/kg of remimazolam (Group R) or 0.3 mg/kg of etomidate (E group) in combination with alfentanil for anesthesia induction. *Results:* The mean arterial pressure (MAP) and heart rate (HR) were significantly higher in the E group compared to Group R ($P < 0.05$). Ephedrine was administered more frequently in the Group R (30%) than in the Group E (10%), with a statistically significant difference ($P = 0.023$). The incidence of myoclonus was markedly lower in the Group R (0%) compared to the Group E (60%, $P < 0.01$). *Conclusion:* During gastroenteroscopy with alfentanil, remimazolam was associated with lower MAP and HR compared to etomidate. Patients receiving remimazolam experienced a higher incidence of post-induction hypotension. Nonetheless, the safety and efficacy of remimazolam were comparable to those of etomidate, supporting its suitability as a sedative for ASA I–II elderly patients undergoing gastrointestinal endoscopy.

Keywords: Etomidate; Remimazolam; Gastroenteroscopy; Elderly patients

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1. Introduction

Gastrointestinal endoscopy is currently regarded as the gold standard for diagnosing disorders of the gastrointestinal tract. However, the procedure can induce symptoms such as nausea, vomiting, abdominal discomfort, and, in some cases, cardiovascular and cerebrovascular complications. Advances in anesthetic techniques and the development of novel anesthetic agents have enabled endoscopic procedures to be performed under sedation, significantly improving patient comfort and satisfaction.

The demand for painless gastrointestinal endoscopy is increasing among older adults. Due to its speed

and efficiency, this procedure places high demands on anesthetic agents. Propofol, widely used for its rapid onset and metabolism, has limitations in maintaining circulatory stability. It may also lead to intraoperative hypotension and respiratory depression, posing risks for elderly outpatients [1].

Remimazolam, a novel ultra-short-acting benzodiazepine sedative targeting GABAA receptors, is characterized by minimal effects on respiratory and cardiovascular systems, rapid onset of action, and quick metabolism [2–4]. It also offers significant advantages for elderly patients with hepatic or renal dysfunction. Studies involving remimazolam in endoscopic procedures and general anesthesia have demonstrated its effectiveness in ensuring a swift recovery and safety [5,6].

Etomidate, an imidazole derivative with potent hypnotic effects and excellent hemodynamic stability, is another option for anesthesia in elderly patients. This study aims to compare the effects of remimazolam and etomidate on hemodynamic stability in patients undergoing gastrointestinal endoscopy.

2. Materials and methods

2.1. Participants

This prospective randomized controlled trial included individuals aged 65 to 80 years with ASA physical status grades I–II, who underwent gastrointestinal endoscopy under anesthesia at the Endoscopy Center of Hebei University Affiliated Hospital from October 2023 to May 2024. The primary objective was to evaluate the impact of remimazolam on hemodynamics in elderly patients. Participants were randomly assigned to one of two sedation protocols through a computer-generated random sequence using a 1:1 allocation ratio. Due to the distinct physical appearances of the two medications, a single-blind design was employed, ensuring that all endoscopists, nurses, and patients were blinded to group assignments. The Ethics Committee of Hebei University Affiliated Hospital approved the study protocol (HDFYLL-KY-2023-023).

Inclusion criteria: (1) ASA Physical Status I–II; (2) Age between 65 and 80 years; and (3) Willingness to undergo painless gastroscopy with an understanding of associated risks.

Exclusion criteria: (1) Allergies to any drugs used in the study; (2) Severe organ dysfunction; (3) Anticipated difficult airway management; (4) Dependence on psychotropic substances; and (5) Refusal to participate.

The sample size was calculated using PASS 11.0 software. Preliminary data indicated that during gastroscopy with remimazolam and etomidate anesthesia, mean arterial pressure [MAP, in mean (standard deviation, SD)] was 80.0 (13) mmHg and 93.0 (18) mmHg, respectively. Assuming a Type I error of 0.05, each group required 42 participants. To account for a 20% dropout rate, 50 participants were selected for each group.

2.2. Study design

Participants observed an eight-hour fasting period prior to the procedure. Upon entering the operating room, standard monitoring included electrocardiogram (ECG), noninvasive blood pressure (NIBP), and peripheral oxygen saturation (SpO_2). Oxygen was administered via mask at a flow rate of 3 L/min. Intravenous cannulation was performed for fluid infusion at 10 ml/kg.

Anesthesia induction began with alfentanil (Yichang Renfu Pharmaceutical Co., Ltd.) at a dose of 5 μg/kg, followed by either etomidate (0.3 mg/kg) (Jiangsu Nhwa Pharmaceutical Co., Ltd., China) administered over 60 seconds for Group E or remimazolam (0.2 mg/kg) (Jiangsu Hengrui Medicine Co., China) administered

over 60 seconds for Group R. The examination commenced once the eyelash reflex disappeared. If patients exhibited signs of frowning or awakening, additional medication was administered intravenously: 0.05 mg/kg of remimazolam for Group R or 0.06 mg/kg of etomidate for Group E.

Anesthesiologists closely monitored all parameters to ensure patient safety during anesthesia. If necessary, medications such as atropine or ephedrine were administered to maintain circulatory stability. Respiratory support, including jaw elevation, was provided when required. Residual drug effects were reversed using flumazenil or naloxone if necessary.

Vital signs were documented at the following time points:

(1) Five minutes prior to anesthesia induction

(2) One and five minutes after the patient lost consciousness

(3) At the end of the examination

All adverse reactions occurring during the perioperative period were recorded.

2.3. Statistical analysis

Experimental data were analyzed using SPSS 20.0 software. Continuous variables were expressed as mean ± standard deviation and compared using *t*-tests. Categorical and ordinal data between the two groups were analyzed using χ^2 tests or Fisher's exact test, as appropriate. A significance level of $P < 0.05$ was applied.

3. Results

A total of 100 patients were initially recruited for the study, with no exclusions; each group comprised 50 participants. There were no significant differences in sex, age, BMI, or ASA classification between the two groups (**Table 1**). All participants successfully achieved sedation.

Table 1. Basic information of patients ($n = 100$)

	Group R	Group E	*P* value
Gender			0.84
Male [*n* (%)]	28 (56%)	30 (60%)	
Female [*n* (%)]	22 (44%)	20 (40%)	
Age (years)	70.62 ± 4.43	71.86 ± 4.73	0.18
BMI (kg/m²)	22.72 ± 1.76	23.04 ± 1.94	0.39
ASA grade			0.83
I	16	14	
II	34	36	

3.1. Hemodynamic parameters

The primary focus of this study was the hemodynamic changes observed between the groups. The MAP was significantly higher in Group E compared to Group R ($P < 0.05$). Heart rates were also higher in Group E compared to Group R. Furthermore, the use of ephedrine was more frequent in Group R (30%) than in Group E (10%), with a statistically significant difference ($P = 0.023$) (**Figures 1** and **2**).

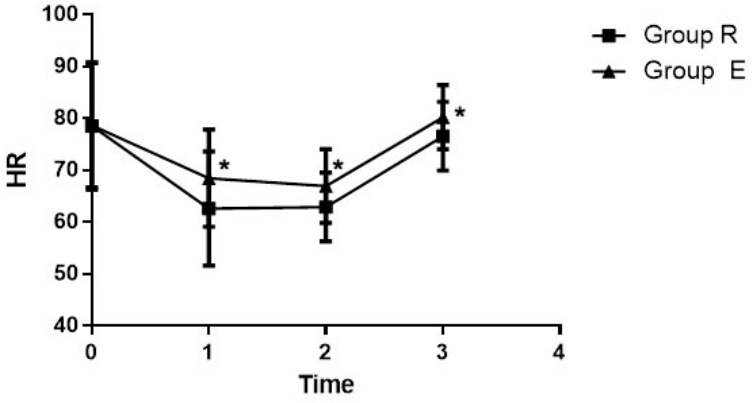

Figure 1. Comparison of heart rates between two groups. Heart rate values were measured at baseline (0), 1 minute after induction (1), 5 minutes after induction (2), and at the end of surgery (3). *$P < 0.05$ vs. Group R

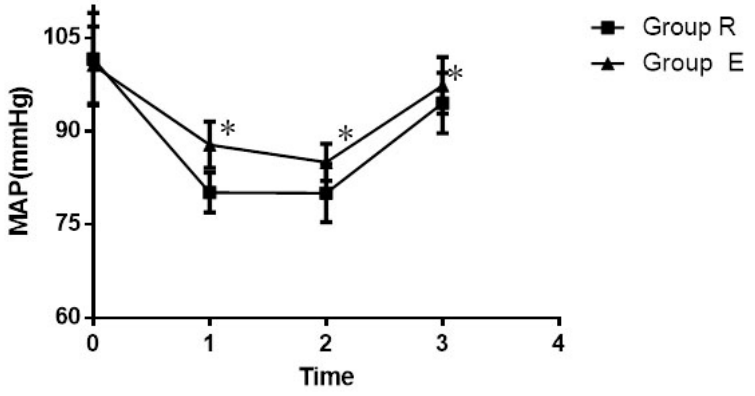

Figure 2. Comparison of mean arterial pressure between the two groups. MAP values were measured at baseline (0), 1 minute after induction (1), 5 minutes after induction (2), and at the end of surgery (3). *$P < 0.05$ vs. Group R

3.2. Secondary outcomes

The occurrence of myoclonus was markedly lower in Group R (0%) compared to Group E (60%), with a significance level of $P < 0.001$ (**Table 2**). Blood oxygen saturation levels did not differ significantly between the two groups ($P > 0.05$) (**Figure 3**). Additionally, no significant differences were observed in the incidence of postoperative adverse reactions, such as nausea and vomiting, between the two groups ($P > 0.05$) (**Table 2**).

Table 2. Adverse reactions ($n = 100$)

Adverse reaction	Group R	Group E	*P* value
Ephedrine usage rate	15 (30%)	5 (10%)	0.023
Myoclonus	0 (0%)	30 (60%)	< 0.001
Nausea and vomiting	2 (5%)	3 (6%)	0.100

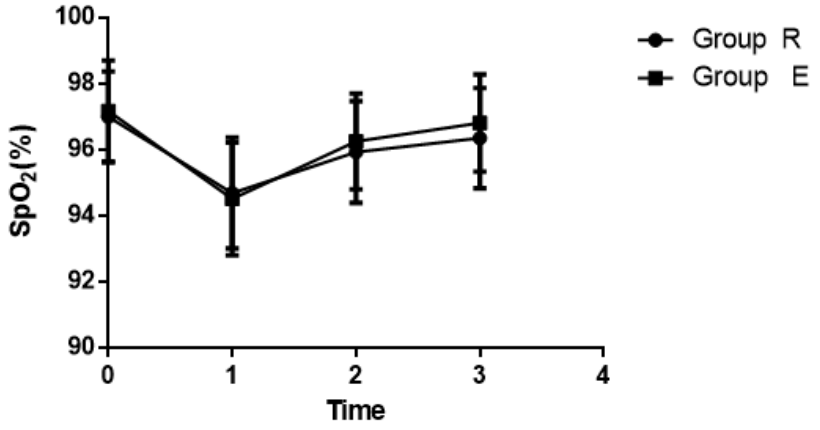

Figure 3. Comparison of blood oxygen saturation between the two groups. Blood oxygen saturation levels were measured at baseline (0), 1 minute after induction (1), 5 minutes after induction (2), and at the end of surgery (3). No statistically significant differences were observed between the two groups.

4. Discussion

With the advancement of medical technology, the population of elderly patients requiring anesthesia is increasing. However, the physiological fragility of this demographic, particularly in organ functions, necessitates anesthetic protocols that minimize impacts on the respiratory and circulatory systems. Painless gastroscopy has gained popularity among older adults, as it enhances patient comfort during diagnostic procedures. The traditional combination of propofol, sufentanil, and midazolam remains a standard for gastrointestinal endoscopy but significantly impacts respiratory and circulatory systems. This combination is not always suitable for older populations, presenting challenges for anesthesiologists tasked with balancing efficacy, safety, and hemodynamic stability.

Etomidate is widely regarded as an appropriate choice for anesthesia induction due to its dependable sedative properties and superior hemodynamic stability, making it suitable for outpatient gastroscopy [7]. Similarly, remimazolam has been shown to exert minimal hemodynamic depression compared to propofol [4]. Both agents are advantageous for patients with unstable hemodynamics. In this study, it was observed that fluctuations in MAP were more pronounced in Group R than in Group E following induction, suggesting that etomidate provides better hemodynamic stability. These findings align with prior studies [8]. This difference may be attributed to the distinct receptor interactions and physiological effects of the two agents, leading to varying impacts on circulatory parameters.

Etomidate's ability to preserve sympathetic tone and autonomic reflexes likely contributes to its circulatory stability during induction [9]. Conversely, intravenous benzodiazepines, such as remimazolam, tend to reduce cardiac output and systemic vascular resistance, subsequently lowering arterial blood pressure. Moreover, remimazolam decreases autonomic nervous activity during the induction phases [10]. When combined with opioids, remimazolam exhibits synergistic effects that further suppress autonomic nervous system activity, potentially compounding its circulatory effects [11].

The incidence of myoclonus observed in Group E was 60%, consistent with previous findings that reported rates between 50% and 80% [12]. Myoclonus can cause postoperative muscle discomfort, elevated intraocular

pressure, and the risk of reflux aspiration in patients with incomplete fasting, potentially resulting in severe complications. While both etomidate and remimazolam demonstrate minimal hemodynamic impact, the high incidence of myoclonus restricts the broader application of etomidate. Conversely, remimazolam's lack of association with myoclonus provides it with a distinct advantage in clinical applications.

4.1. Limitations

This study has several limitations. Firstly, it focused solely on outpatient cases, where preoperative preparations may not match the rigor of inpatient evaluations. Secondly, the study was limited to short procedures, such as gastroscopy, and did not include long-term hemodynamic monitoring, potentially introducing bias regarding prolonged anesthesia outcomes. Lastly, the single-center design and relatively small sample size may limit the generalizability of the findings. To improve reliability, future research should involve larger sample sizes and multi-center studies to validate these results.

5. Conclusion

In the context of gastroenteroscopy with alfentanil, remimazolam was associated with a reduction in mean arterial pressure (MAP) and heart rate compared to etomidate. Patients receiving remimazolam exhibited a higher incidence of post-induction hypotension. Nevertheless, the safety and efficacy of remimazolam were found to be comparable to those of etomidate, establishing it as a viable option for sedation in ASA I-II elderly patients undergoing gastrointestinal endoscopy.

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Disclosure statement

The authors declare no conflict of interest.

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