

Effect of Oliceridine Pretreatment on Etomidate-Induced Myoclonus: A Proof-of-Concept Randomized Trial

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Purpose: Etomidate offers hemodynamic stability for anesthesia induction but frequently causes myoclonus. This study evaluated oliceridine, a G-protein biased μ -opioid receptor agonist, for prevention of etomidate-induced myoclonus.

Patients and Methods: In this double-blind, randomized trial, patients scheduled for elective general anesthesia were allocated to receive either intravenous oliceridine 0.03 mg/kg (Group O) or an equivalent volume of normal saline (Group NC) 5 minutes before anesthesia induction with 0.3 mg/kg etomidate administered over 30–60s. The primary outcome was the incidence of myoclonus within 2 minutes after etomidate administration. Secondary outcome was the severity of myoclonus. Perioperative hemodynamic variables, the incidence of adverse events and postoperative pain intensity (assessed using the Numerical Rating Scale) were recorded.

Results: Of 93 patients who completed the study, Group O showed lower myoclonus incidence (10.9% vs 57.4%; $P < 0.001$), with relative risk 0.189 (95% CI: 0.080–0.421) and the number needed to treat 2.147 (95% CI: 1.495–3.222). No severe myoclonus occurred in Group O (vs 2.1% in NC), with fewer mild-moderate cases. On postoperative day 1, Group O also had lower pain scores both at rest (0.9 ± 0.8 vs 1.3 ± 0.9 ; $P = 0.020$) and during activity (1.2 ± 1.1 vs 1.8 ± 1.1 ; $P = 0.017$). Hemodynamic variables were comparable, and no significant differences in adverse events were detected between groups.

Conclusion: In this single-center proof-of-concept randomized trial of ASA I–II patients, pretreatment with oliceridine (0.03 mg/kg) before etomidate induction reduced the incidence of etomidate-induced myoclonus. The statistically lower postoperative day 1 pain scores in the oliceridine group should be interpreted cautiously, and these findings warrant confirmation in larger multicenter trials involving broader patient populations.

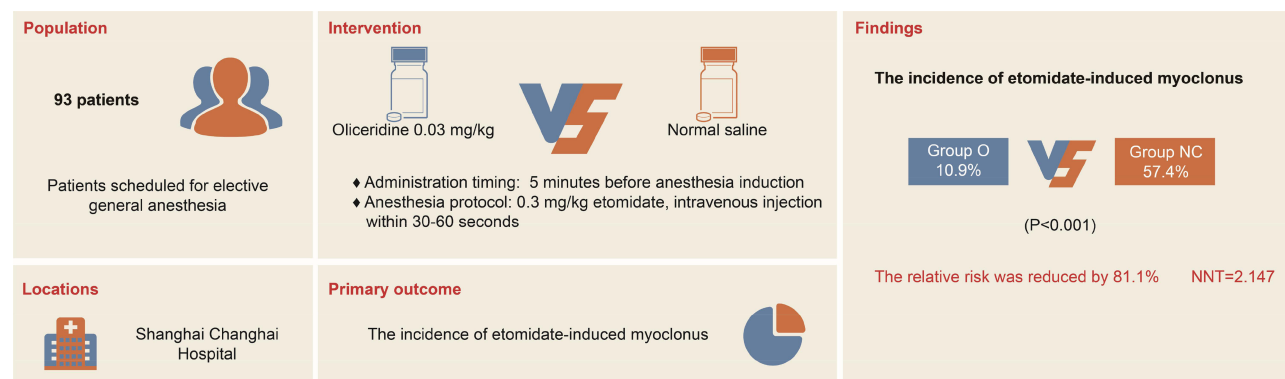
Keywords: oliceridine, etomidate, myoclonus, pretreatment, intravenous anesthesia, analgesia

Introduction

Etomidate, an imidazole carboxyl group derivative, is one of the most widely used inducing agents for intravenous general anesthesia because of its hemodynamic stability and minimal respiratory depression. However, it often triggers myoclonus, with an incidence rate of 50–80%.^{1,2} Myoclonus, characterized by sudden, brief, involuntary muscle jerks of nervous origin, differs from fasciculations or cramps,³ and may lead to complications such as muscle injury, hyperkalemia, increased intraocular pressure, and aspiration risk.⁴ Therefore, reducing the incidence of myoclonus is crucial to minimize aspiration risk, intraocular pressure elevation, and other adverse events, thereby enhancing the safety of anesthetic induction.

Various pharmacological strategies have been proposed to prevent etomidate-induced myoclonus, including dexmedetomidine, non-depolarizing neuromuscular blocking agents, magnesium sulfate, benzodiazepines, and opioids.^{2,5–7}

Graphical Abstract



Among these, opioids have consistently demonstrated robust efficacy.^{2,8,9} Nevertheless, the use of conventional opioids is often limited by dose-dependent adverse effects such as respiratory depression, chest wall rigidity, cough, and hemodynamic instability, which may be undesirable during anesthetic induction.^{6,10} In this context, novel opioid receptor agonists with improved safety profiles are urgently needed to refine anesthesia induction protocols.

Oliceridine is a first-in-class biased μ -opioid receptor agonist that preferentially activates G-protein signaling over β -arrestin pathways, potentially reducing common opioid-related adverse effects such as respiratory depression and hemodynamic instability while preserving analgesic efficacy.^{11,12} Recent evidence also suggests that oliceridine may attenuate sufentanil-induced cough during anesthetic induction.¹³ More recently, emerging evidence has indicated that oliceridine may also reduce the incidence of etomidate-induced myoclonus.¹⁴ Notably, our study was conducted independently and contemporaneously. However, the available evidence remains limited, and further well-designed randomized controlled trials are warranted to confirm these findings and better characterize its clinical utility. Therefore, we conducted this proof-of-concept randomized trial to evaluate whether pretreatment with oliceridine can reduce the incidence of etomidate-induced myoclonus compared with placebo in adults undergoing general anesthesia, with the goal of informing its potential perioperative utility as a safer opioid option.

Materials and Methods

Design and Patients

This study was a prospective, interventional proof-of-concept trial at the First Affiliated Hospital of Naval Medical University. The study protocol was approved by the Ethics Committee of the hospital (approval no. CHEC2025-218) and registered in the Chinese Clinical Trial Registry (ChiCTR NO. ChiCTR2500104733) on June 23, 2025 before patient enrollment, adhering to international standards. Written informed consent was obtained from all patients or their legally authorized representatives. The study was conducted in accordance with the Declaration of Helsinki and the manuscript was written according to the CONSORT reporting guidelines.¹⁵

The study included patients aged 18–65 years, with an American Society of Anesthesiologists (ASA) physical status of I or II, who were scheduled for elective surgery under general anesthesia. The exclusion criteria were as follows: body mass index (BMI) $> 30 \text{ kg/m}^2$; adrenal cortical insufficiency; neurological and psychiatric diseases; known allergy to any drug in the study; severe hepatic, renal, pulmonary, or cardiovascular impairment, use of analgesics, sedatives, opioids within 24 hours prior to the study initiation and participation in another clinical trial.

Randomization and Blinding

A statistician, who was blinded to the allocation process, used the SPSS software (version 29, SPSS Inc.) to generate the allocation sequence through block randomization with a block size of 4. Patients were randomly assigned in a 1:1 ratio to

either the oliceridine group (Group O; Jiangsu Nhwa Pharmaceutical Co., Ltd.) or the normal saline group (Group NC). The randomization results were concealed in sequentially numbered, opaque, sealed envelopes. These envelopes were securely stored and managed by a dedicated research coordinator who was not involved in patient enrollment, anesthesia procedures, or outcome assessment. The envelopes were opened only after a patient had completed all eligibility assessments and was formally confirmed to be enrolled into the trial, immediately before the start of anesthesia induction. This research coordinator, who was not involved in clinical management, prepared the study drugs according to group allocation, ensuring identical appearance and a final volume of 5 mL in all syringes, and labeled them uniformly as “Trial”. After preparation, the study drug was transferred directly to the attending anesthesiologist without any disclosure of group allocation to involved clinical staff.

This study had a double-blind design throughout the trial process. Both the patients and the attending anesthesiologist remained blinded to the group assignments. This single attending anesthesiologist, who was blinded to group allocation and not involved in group assignment, drug preparation, or postoperative follow-up, performed the anesthesia induction, managed the surgical procedure, and evaluated the myoclonus and hemodynamic parameters, thereby minimizing the risk of observer bias in the assessment of myoclonus severity and hemodynamic changes. This blinding remained intact throughout the study, except in emergencies that necessitated unblinding. Furthermore, the statisticians responsible for analyzing the data were also blinded to the group allocations, ensuring an objective assessment and comparison of outcomes.

Anesthesia and Perioperative Nursing

All patients adhered to standard preoperative fasting guidelines, with no premedication administered. Standard monitoring was established upon arrival in the operating room, including blood pressure, electrocardiography (ECG), peripheral oxygen saturation monitoring (SpO₂) and pressure of exhaled carbon dioxide (PetCO₂). The patients received lactated Ringer’s solution throughout the procedure via a 20 - gauge intravenous catheter.

After 3 minutes of preoxygenation (6 L/min), Group O received intravenous oliceridine (0.03 mg/kg) while Group NC received equivalent normal saline, followed 5 minutes later by etomidate (0.3 mg/kg; Jiangsu Nhwa Pharmaceutical Co., Ltd.) administered over 30–60 seconds. Myoclonus was assessed 2 minutes after induction. Two minutes after the observation, all patients received rocuronium (0.6 mg/kg) and sufentanil (0.3 µg/kg) to facilitate tracheal intubation.

Anesthesia was maintained using a balanced inhalation-intravenous technique, with the administration of muscle relaxants, analgesics, and sedatives individually tailored by the attending anesthesiologist based on the patient’s clinical status and surgical stimuli. Sevoflurane (0.7–1.0 MAC) was inhaled in combination with propofol (2–4 mg/kg/h) and remifentanyl (0.1–0.3 µg/kg/min) to sustain anesthetic depth, which was monitored and adjusted to maintain a bispectral index value between 40 and 60. Mechanical ventilation was regulated to maintain PetCO₂ between 35–45 mmHg. Residual neuromuscular blockade was reversed with neostigmine and glycopyrronium as required.

Hemodynamic deviations were treated as part of predefined intervention thresholds: hypotension (systolic blood pressure [SBP] < 90 mmHg or > 25% decrease from baseline, or diastolic blood pressure [DBP] < 50 mmHg), with ephedrine 6 mg; for hypertension (SBP > 180 mmHg or > 25% increase from baseline, or DBP > 100 mmHg) with urapidil 5 mg; bradycardia (heart rate [HR] < 45 bpm or > 25% decrease) was treated with atropine 0.5 mg, and tachycardia (HR > 120 bpm or > 25% increase) with esmolol 10 mg.

Outcome Measurements

The primary outcome was the incidence of myoclonus within 2 minutes after the administration of etomidate.

Secondary outcomes included the severity of etomidate-induced myoclonus, which was graded on a 4 - point scale: 0 (none), 1 (mild, movement at the finger or wrist only), 2 (moderate, involving the face or legs), or 3 (severe, generalized response or fast limb abduction).⁵

Baseline data included demographic characteristics, preoperative laboratory investigations, and pertinent comorbidities. Adverse drug reactions (such as dizziness, nausea, vomiting, hypotension, bradycardia, pruritus, respiratory depression, and hallucinations) were also recorded. Hemodynamic stability was judged by change of mean arterial pressure (MAP) and HR at four time points: baseline (T0), 5 minutes after study drug administration (T1), 5 minutes after anesthesia induction (T2), and 5 minutes after the start of surgery (T3). Postoperative follow-up included time to

extubation in the post-anesthesia care unit (PACU), pain intensity at PACU discharge (assessed using the Numeric Rating Scale, NRS), and pain scores at rest and during movement on postoperative day 1. Additionally, patients were evaluated for unpleasant memories related to the induction phase and the presence of postoperative myalgia.

Sample Size Calculation

Based on previous studies, the incidence of etomidate-induced myoclonus in the Group NC was estimated to be 70%.^{1,2,16} Sample size calculations were performed using PASS software (Stata Corp. LP). Assuming a reduction of 40% in Group O, with $\alpha = 0.05$, and 90% power, 96 patients (48 per group) were required, accounting for a 10% withdrawal rate.

Statistical Analysis

Statistical analyses were performed using SPSS software package version 30.0 (SPSS Inc.) the statistical software packages R (<http://www.R-project.org>, The R Foundation) and Free Statistics software version 2.2 and GraphPad Prism version 10.6.0 (GraphPad Software, Inc.) Normally distributed continuous data will be presented as mean $\pm$ standard deviation (SD) and compared using Student's *t*-test or one-way analysis of variance (ANOVA). Categorical variables will be expressed as frequencies and percentages and analyzed using the chi-square test or Fisher's exact test. Repeated-measures ANOVA will be used for hemodynamic variables. Relative risk (RR) was defined as the experimental event rate divided by the control event rate. Unadjusted RRs and 95% confidence intervals (CIs) were estimated using a log-binomial regression model. Number needed to treat (NNT) was defined by $1/(\text{Control Event Rate} - \text{Experimental Event Rate})$.

For missing data, primary outcome data were complete for all included patients, ensuring full analysis of myoclonus incidence. Secondary outcomes had minor missing values, which were handled using multiple imputation by chained equations in R. Because this was a proof-of-concept randomized trial focused on the prespecified primary outcome, no formal adjustment for multiple comparisons was performed. Analyses of secondary outcomes were considered exploratory, and the corresponding *P* values were interpreted as descriptive only. Statistical significance was defined as a two-sided *P*-value of < 0.05 .

Results

Patient recruitment and data collection occurred from June to December 2025, during which 96 patients were assessed for enrollment. Of these, 93 were included in the final analysis (46 vs 47): One patient declined to participate, and two were excluded due to severe clinical conditions requiring planned postoperative ICU admission (Figure 1). The two groups were well balanced with respect to baseline demographics, comorbidities, laboratory parameters, and disease categories (Table 1).

The incidence of etomidate-induced myoclonus was 10.9% in Group O and 57.4% in Group NC ($P < 0.001$). Pretreatment with oliceridine significantly reduced the risk of myoclonus by 81% compared to Group NC (RR = 0.189; 95% CI: 0.080–0.421). This absolute risk reduction resulted in a NNT of 2.147 (95% CI 1.495–3.222). In other words, treating approximately three patients with oliceridine prevents one episode of etomidate-induced myoclonus (Table 2). Myoclonus severity also differed significantly between groups. 6.5% of Group O patients had mild myoclonus (27.7% in Group NC), 4.3% had moderate myoclonus (27.7% in Group NC), and no severe myoclonus was detected in Group O, versus 2.1% in Group NC (Figure 2).

There were no statistically significant between-group differences in the incidence of adverse events, with dizziness occurring in 10.9% vs 4.3% of patients ($P = 0.267$); no cases of nausea, vomiting, hypotension, bradycardia, pruritus, respiratory depression, or hallucinations were noted in either group. Perioperative anesthetic management was also comparable between groups (Table 2). Furthermore, perioperative vital signs (HR, MAP, and SpO₂) remained stable and comparable between groups throughout the observation period (T0 to T3), with no statistically significant differences detected at any time point (Figure 3). Postoperatively, extubation time and NRS at PACU discharge did not differ. However, on postoperative day 1, patients in Group O reported lower pain scores both at rest (0.9 ± 0.8 vs 1.3 ± 0.9 ; $P = 0.020$) and during movement (1.2 ± 1.1 vs 1.8 ± 1.1 ; $P = 0.017$). Muscle soreness was reported in three patients (6.5%) in Group O and none in Group NC ($P = 0.117$). The analgesic and antiemetic use did not differ significantly (Table 3).

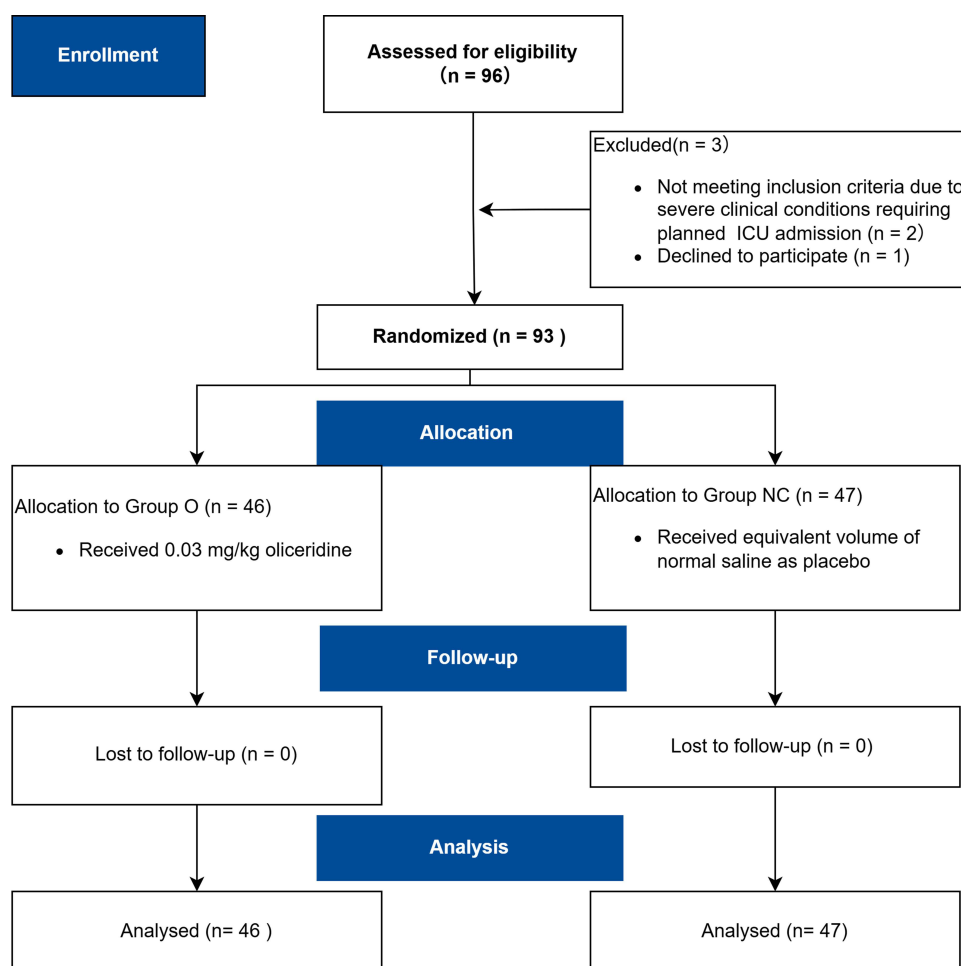


Figure 1 Study flow diagram.

Abbreviations: ICU, intensive care unit; NC, normal saline; O, oliceridine.

Discussion

As a proof-of-concept investigation, our results provide initial evidence that pretreatment with this G-protein biased μ -opioid receptor agonist can mitigate the incidence and severity of myoclonus during anesthesia induction (10.9% vs 57.4%; RR = 0.189; 95% CI: 0.080–0.421; $P < 0.001$), with the NNT of 2.147 (95% CI: 1.495–3.222). Furthermore, postoperative day 1 pain scores (at rest and during movement) were lower in Group O, but the difference was small and of uncertain clinical relevance given the exploratory nature of this secondary outcome.

Table 1 Baseline Characteristics

	Group O (n = 46)	Group NC (n = 47)
Age (y)	53.2 ± 8.0	52.1 ± 11.0
Sex – Female, n (%)	18 (39.1)	23 (48.9)
BMI (kg/m ²)	23.0 ± 3.4	23.5 ± 3.0
Comorbidities, n (%)		
Hypertension	12 (26.1)	15 (31.9)
Diabetes	3 (6.5)	9 (19.1)
CAD	1 (2.2)	0 (0)

(Continued)

Table 1 (Continued).

	Group O (n = 46)	Group NC (n= 47)
Laboratory parameters		
Hemoglobin (g/L)	127.7 ± 18.3	124.8 ± 23.2
Creatinine (μmol/L)	63.9 ± 17.3	63.8 ± 14.3
ALT (U/L)	20.0 (16.0, 33.5)	17.0 (14.5, 26.5)
AST (U/L)	21.0 (18.0, 34.0)	18.0 (16.0, 25.5)
ASA status (I/II)	6/40	6/41
Disease Category, n (%)		
Upper Gastrointestinal	2 (4.3)	1 (2.1)
Lower Gastrointestinal	32 (69.6)	32 (68.1)
Urology	4 (8.7)	1 (2.1)
Gynecology	7 (15.2)	13 (27.7)
Breast Surgery	1 (2.2)	0 (0)

Notes: Data are presented as mean ± SD or median (IQR) for continuous variables, and as frequencies (percentages) for categorical variables.

Abbreviations: ALT, alanine aminotransferase; AST, aspartate aminotransferase; ASA, American Society of Anesthesiologists; BMI, body mass index; CAD, coronary artery disease; IQR, Interquartile Range; NC, normal saline; O, oliceridine; SD, standard deviation.

Table 2 Etomidate-Induced Myoclonus, Adverse Events and Procedure Details

	Group O (n = 46)	Group NC (n= 47)	P value
Etomidate-Induced Myoclonus			
Total frequency, n (%)	5 (10.9)	27 (57.4)	< 0.001
Relative risk (95% CI) [#]	0.189 (0.080–0.421)	(Reference)	–
NNT (95% CI)	2.147 (1.495–3.222)	–	–
Adverse Events			
Dizziness, n (%)	5 (10.9)	2 (4.3)	0.267
Nausea, n (%)	0	0	NA
Vomiting, n (%)	0	0	NA
Hypotension, n (%)	0	0	NA
Bradycardia, n (%)	0	0	NA
Pruritus, n (%)	0	0	NA
Respiratory Depression, n (%)	0	0	NA
Hallucination, n (%)	0	0	NA
Procedure details			
Etomidate induction dose (mg)	19.1 ± 3.7	19.5 ± 3.2	0.556
Consumption of sufentanil (μg)	0.0 ± 0.2	1.5 ± 7.3	0.17
Consumption of remifentanyl (mg)	0.9 ± 0.6	1.0 ± 0.7	0.468
Consumption of oliceridine (mg)	5.3 ± 1.8	6.1 ± 4.5	0.33
Surgery time (min)	148.8 ± 84.9	128.8 ± 74.6	0.242

Notes: Data are presented as mean ± SD for continuous variables, and as frequencies (percentages) for categorical variables. [#]Relative risk – 95% CI calculated from log-binomial model; Relative risk were unadjusted. P values were calculated using the Fisher's exact test or independent samples t-test.

Abbreviations: CI, confidence interval; NA, Not applicable (no events occurred in either group; statistical comparison could not be performed); NC, normal saline; NNT, number needed to treat; O, oliceridine; SD, standard deviation.

Etomidate-induced myoclonus remains common, occurring in 50–80% of patients even with modern formulations.¹⁷ In earlier reports, rapid bolus administration (0.3 mg/kg over a period of 30s) yielded myoclonus rates of 62% and 75.9%,^{16,18} while 83.3% of young (30–40 years) ASA I patients undergoing plastic surgery developed myoclonus.¹⁹ Clinical observations suggest that injection speed, patient age, and etomidate dose influence the development of myoclonus, with faster administration and younger age being associated with a higher risk.²⁰ In our study, etomidate was injected more slowly, over 30–60s,

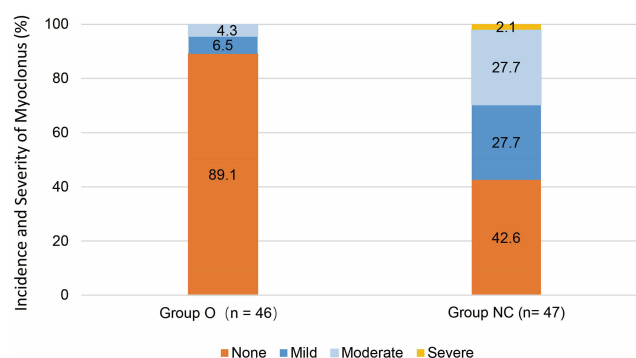


Figure 2 Incidence and severity of etomidate-induced myoclonus. The bar graph shows the incidence and severity of myoclonus in Group O (n = 46) and Group NC (n = 47). The bars are stacked, with “None” at the bottom, followed by “Mild”, “Moderate”, and “Severe” at the top. The y-axis represents the percentage.

Abbreviations: NC, normal saline; O, oliceridine.

and the enrolled patients were older (50–60 years) with ASA physical status I–II. These differences in administration and patient characteristics likely contributed to the lower incidence in Group NC (57.4%).

As a new G-protein biased μ -opioid receptor (MOR) agonist, oliceridine markedly reduced the incidence of etomidate-induced myoclonus in this study, with an observed rate of 10.9%, consistent with previous reports showing a protective effect of opioids.^{2,8,9} This rate is comparable to the 10.5% reported in a meta-analysis of butorphanol versus placebo,¹ which is lower than the 22.2% pooled estimate for various opioids (remifentanyl, fentanyl, alfentanil, sufentanil, butorphanol, and dezocine),⁸ yet higher than the 3.8% observed with remifentanyl alone.²¹ These findings indicate that the effectiveness of opioids in preventing etomidate-induced myoclonus may vary among the agents. Such variability may be related to the mechanisms of etomidate-induced myoclonus; however, the underlying mechanisms remain unclear.

To better understand this variability, some studies have suggested that etomidate-induced myoclonus may reflect an underlying state of neocortical hyperexcitability, primarily related to increased glutamatergic activity and impaired inhibitory control.^{22,23} Given that MOR activation inhibits presynaptic calcium influx and thereby limits glutamate release, it is plausible that oliceridine attenuates myoclonus by dampening this excitatory surge.²⁴ Although direct neurochemical evidence is lacking, the observed reduction in myoclonus following pretreatment with oliceridine and other opioids supports this hypothesis.

Oliceridine exhibits reduced MOR internalization and phosphorylation at serine 375 compared with morphine and demonstrates approximately threefold greater selectivity for G protein-mediated signaling over β -arrestin pathways relative to both morphine and fentanyl.²⁵ The favorable kinetic profile of oliceridine, including rapid onset (2–5 min) and preserved efficacy in elderly or renally impaired patients, further supports its suitability and safety as a pretreatment agent in this context.^{11,12}

Beyond myoclonus prevention, we observed statistically lower pain scores on postoperative day 1 in Group O. However, the absolute difference was small (0.4–0.6 points) and did not reach the minimal clinically important difference of 1 point.^{26,27} Given the limited clinical significance and the exploratory nature of this secondary outcome, this finding should be interpreted cautiously. While this observation aligns with the known analgesic efficacy of opioid agonists,²⁸ the short half-life of oliceridine makes a sustained postoperative analgesic effect uncertain. In addition, given the single-center design, limited sample size, and exploratory of secondary outcomes in this proof-of-concept trial, this finding may be attributable to random variation. Moreover, no formal adjustment for multiple comparisons was applied in this trial, which may increase the risk of type I error, particularly for secondary outcomes. Therefore, findings related to secondary outcomes should be regarded as exploratory and require confirmation in larger confirmatory trials.

While most prior studies have evaluated operative analgesia,^{11,29} its use as a preoperative pretreatment agent remains scarcely explored. A recent study demonstrated that oliceridine pretreatment could attenuate sufentanil-induced cough, yet it did not assess postoperative outcomes.^{13,14} Aligning with this finding, our study further corroborates the safety and potential utility of the pretreatment strategy.

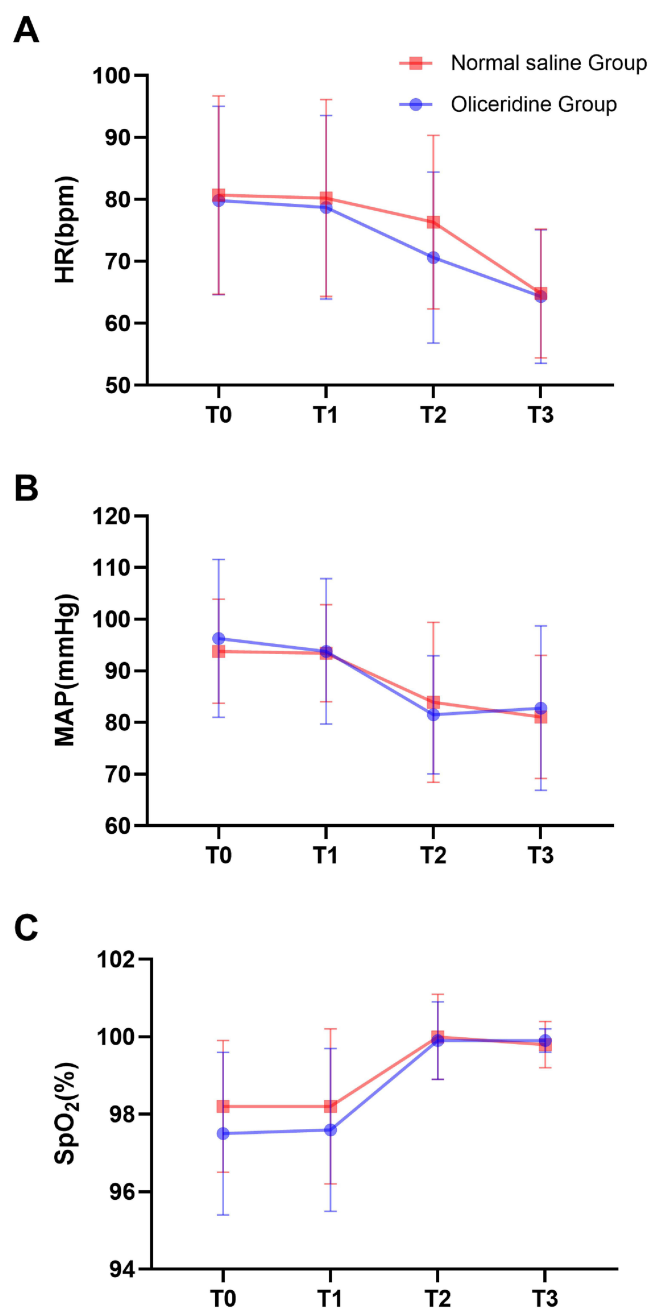


Figure 3 Changes of vital signs. Data are expressed as mean (standard deviation). **(A)** Heart rate (HR, beats per minute). **(B)** Mean arterial pressure (MAP, mmHg). **(C)** Oxygen saturation (SpO₂, %). Red line: Normal saline group. Blue line: Oliceridine group. T0: baseline; pre-operation. T1: 5 minutes after study drug administration. T2: 5 minutes after anesthesia induction. T3: 5 minutes after the start of surgery. No statistically significant differences were found between groups (repeated measures ANOVA).

Abbreviations: HR, Heart rate; MAP, mean arterial pressure; SpO₂, oxygen saturation.

Regarding safety outcomes, the incidence of dizziness was numerically higher in the Group O (5/46 vs 2/47), but the difference was not statistically significant ($P = 0.267$), which is consistent with previous studies.⁸ Notably, two patients in Group NC also reported dizziness, which may be partly attributable to a placebo effect. In addition, the use of a structured, option-based inquiry (eg, asking about dizziness, nausea, vomiting, or hallucinations) rather than an open-ended question may have increased the likelihood of reporting symptoms. No other prespecified adverse events were observed in this small sample. Three patients in Group O reported muscle soreness within 24 h postoperatively. Given the small number of events and the lack of statistical power, this finding cannot be reliably attributed to the study drug and is more likely due to random

Table 3 Postoperative Outcomes

	Group O (n = 46)	Group NC (n= 47)	P value
PACU			
Extubation time (min)	17.1 ± 12.1	16.8 ± 8.8	0.873
NRS at PACU discharge	2.3 ± 1.7	2.4 ± 1.4	0.720
Postoperative day 1			
Muscle soreness, n (%)	3 (6.5)	0 (0)	0.117
NRS at rest	0.9 ± 0.8	1.3 ± 0.9	0.020
NRS during movement	1.2 ± 1.1	1.8 ± 1.1	0.017
Usage of analgesic drugs	25 (54.3)	30 (63.8)	0.352
Usage of antiemetic drugs	0 (0)	1 (2.1)	>0.999

Notes: Data are presented as mean ± SD for continuous variables, and as frequencies (percentages) for categorical variables. P values were calculated using the Fisher's exact test or independent samples t-test.

Abbreviations: NRS, numerical rating scale; NC, normal saline; O, oliceridine; PACU, post-anesthesia care unit; SD, standard deviation.

variation in a small sample. Overall, all safety-related findings from this proof-of-concept trial should be regarded as exploratory, and larger studies are needed to adequately assess the safety profile of oliceridine in this setting.

This study has several limitations. First, as an exploratory proof-of-concept trial, we employed a saline-controlled design to establish the efficacy of oliceridine. While this approach confirmed a significant protective effect, the lack of a positive comparator (eg, fentanyl or dexmedetomidine) prevents a direct assessment of its relative clinical utility, necessitating future head-to-head trials. Nevertheless, our data provide a preliminary reference: the observed myoclonus incidence of 10.9% is lower than the historical ranges reported for fentanyl (32–52.5%),^{30–32} or dexmedetomidine (26–40%).^{7,33} Coupled with its more favorable respiratory safety profile and evidence that it may reduce sufentanil-induced cough,¹³ this suggests oliceridine has potential utility as a safer pre-induction medication. Second, the enrolled patients predominantly underwent abdominal surgery, which may limit the generalizability of our findings to other surgical settings. This patient distribution reflects the clinical practice pattern of our center and resulted in a relatively homogeneous surgical population. Third, the single-center design and relatively small sample size may restrict external validity. However, a recent independently randomized study reported comparable findings,¹⁴ with a myoclonus incidence of 13.3% in the oliceridine group, supporting the consistency of the observed effect. Larger multicenter trials are warranted to confirm these results. Fourth, oliceridine was administered at a fixed dose of 0.03 mg/kg without dose-ranging evaluation; therefore, the optimal pretreatment dose for myoclonus prevention or postoperative analgesia remains to be determined.

Conclusions

In summary, pretreatment with oliceridine at a dose of 0.03 mg/kg attenuates the incidence and severity of etomidate-induced myoclonus, supporting its potential role as an adjunct during anesthetic induction. The statistically lower pain scores observed on postoperative day 1 in unadjusted analyses did not reach the minimal clinically important difference and should be interpreted as exploratory. Therefore, larger confirmatory trials are warranted.

Abbreviations

ANOVA, analysis of variance; ASA, American Society of Anesthesiologists; BMI, body mass index; CI, confidence interval; DBP, diastolic blood pressure; ECG, electrocardiography; Group NC, normal saline group; Group O, oliceridine group; HR, heart rate; ICU, Intensive Care Unit; MAC, minimum alveolar concentration; MAP, mean arterial pressure; MOR, μ -opioid receptor; NNT, number needed to treat; NRS, Numeric Rating Scale; PACU, Post-anesthesia Care Unit; PetCO₂, pressure of exhaled carbon dioxide; RR, relative risk; SBP, systolic blood pressure; SD, standard deviation; SpO₂, peripheral oxygen saturation.

Data Sharing Statement

The datasets generated and/or analyzed during the current study are not publicly available due to institutional restrictions but are available from Lulong Bo upon reasonable request.

Ethics Approval and Informed Consent

This study was registered at the Chinese Clinical Trials Registry (ChiCTR2500104733) on 06/23/2025, and the Ethics Committee of Shanghai Changhai Hospital approved the study (CHEC2025-218). All the participants provided written informed consent.

Consent for Publication

Individual consent was obtained from all participating patients.

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Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

No potential conflict of interest relevant to this article was reported.

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