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Clinical Applications of Oliceridine: Current Research Status, Progress, and Outlook

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Abstract

Oliceridine (TRV-130) is the first G protein-biased μ-opioid receptor (MOR) agonist approved by the U.S. FDA for marketing; it was approved in 2020 for the treatment of moderate-to-severe acute pain in adults. Unlike traditional opioids, oliceridine achieves a dissociation between analgesic effects and opioid-related adverse reactions by preferentially activating G protein signaling pathways and reducing β-arrestin 2 recruitment. In recent years, with the approval of oliceridine in China and the conduct of multiple clinical studies, evidence supporting its use in areas such as postoperative pain management, pain-free endoscopy, and outpatient surgery has continued to accumulate. Based on existing clinical evidence, this article provides a systematic review of the pharmacological characteristics, clinical research progress, and key unresolved issues regarding oliceridine, with the aim of offering guidance for rational clinical use and future research.

Keywords

Oliceridine, Selective μ-Opioid Receptor Agonist, Postoperative Nausea and Vomiting, Acute Pain, Anesthesia

Abbreviations

FDA: Food and Drug Administration; MOR: μ-Opioid Receptor; TRV-130: Oliceridine.

Introduction

Opioids are the cornerstone of treatment for moderate-to-severe acute pain, but their clinical use has long been hampered by adverse reactions such as respiratory depression, nausea and vomiting, constipation, tolerance, and addiction. The molecular basis of these adverse reactions is related to two downstream signaling pathways that are simultaneously activated upon activation of the μ-opioid receptor (MOR): the G-protein pathway primarily mediates analgesic effects, while the β-arrestin pathway is associated with adverse reactions such as respiratory depression and constipation [1]. Based on this theory, the development of G-protein-biased MOR agonists has become a key area for breakthroughs in the field of opioids [1].

It is against this backdrop that oliceridine emerged as the first approved G protein-biased μ-opioid receptor agonist. In August 2020, the U.S. FDA approved oliceridine (brand name OLINVYK™) for the treatment of moderate-to-severe acute pain in adults [1]. In China,

Jiangsu Enhua Pharmaceutical has obtained the exclusive license for the development and commercialization of oliceridine. In recent years, as oliceridine has been progressively adopted in clinical settings both domestically and internationally, a large number of studies have focused on its efficacy and safety across different surgical procedures and patient populations, providing an increasingly robust body of evidence to support its clinical application [2-5]. This article aims to systematically review the pharmacological characteristics and current state of clinical research on oliceridine, as well as to analyze gaps in the current evidence and identify future research directions.

Pharmacological Characteristics

Biased Signal Transduction Mechanism:

Oliceridine is a novel small-molecule intravenous μ-opioid receptor agonist, whose core innovation lies in "biased signal transduction" [1]. Traditional opioids, such as morphine, fentanyl, and sufentanil, activate the μ-opioid receptor (MOR); they produce analgesic effects via the G-protein-coupled pathway while also mediating adverse reactions, such as respiratory depression, constipation, and tolerance, through the β-arrestin pathway. Oliceridine stabilizes a specific conformation of MOR, preferentially activating the G-protein-coupled signaling pathway while significantly reducing the recruitment of β-arrestin 2 [1].

The theoretical advantage of this mechanism lies in achieving a "functional separation" between analgesia and adverse effects, providing reliable analgesia while reducing the incidence of opioid-related adverse effects. Preclinical studies and early Phase III clinical trials have confirmed that the analgesic effects of oliceridine are comparable to those of morphine, but with fewer adverse effects such as respiratory depression and constipation [3].

Pharmacokinetic Characteristics:

Oliceridine takes effect rapidly after intravenous administration and has a short distribution half-life, making it suitable for intraoperative and postoperative acute pain management. Its analgesic effect is dose-dependent, exhibiting a good dose-response relationship across a range of doses [6]. Oliceridine is primarily metabolized by CYP3A4 and CYP2D6; it undergoes N-dealkylation to form primary amine metabolites, which are subsequently glucuronidated after further oxidation to form inactive metabolites, allowing for safe use in patients with impaired hepatic or renal function [7]. It should be noted that the optimal effective dose of oliceridine varies across different clinical settings [6], and this topic will be discussed separately in subsequent sections.

Current Status of Clinical Application Research

Postoperative Pain Management:

Postoperative pain is the primary area of application for oliceridine. Several randomized controlled trials have systematically compared the efficacy and safety of oliceridine with those of sufentanil in postoperative analgesia for various types of surgery.

Thoracic Surgery:

In patients undergoing thoracoscopic lung surgery, a randomized controlled trial conducted by Cai et al. (2026) compared the efficacy of oliceridine and sufentanil for postoperative analgesia in elderly patients. The results showed that the oliceridine group provided satisfactory analgesia while exhibiting a significantly lower incidence of nausea and vomiting [2]. A randomized, double-blind, controlled trial by Hu et al. (2026) in patients undergoing thoracoscopic lobectomy further confirmed that oliceridine was superior to sufentanil in terms of the quality of postoperative recovery and opioid-related adverse events [8].

Abdominal and Breast Surgery:

Lu et al. (2026) conducted a double-blind, randomized controlled trial in patients undergoing modified radical mastectomy and found that the incidence of postoperative nausea and vomiting (PONV) was significantly lower in the oliceridine group than in the sufentanil group [4,8]. A study by Rao et al. (2026) in patients undergoing laparoscopic cholecystectomy demonstrated that oliceridine was superior to sufentanil in terms of the quality of postoperative recovery [9]. Luo et al. (2025) reported a protocol for an ongoing multicenter randomized controlled trial (EOSPONVAS) designed to systematically evaluate the effects of oliceridine and sufentanil on PONV during abdominal

surgery [10]. In addition, Xu et al. (2025) reported an ongoing randomized, double-blind, controlled trial protocol comparing the intraoperative analgesic effects and impact on PONV of oliceridine versus fentanyl in women undergoing laparoscopic cholecystectomy [11].

Meta-Analysis Evidence:

A systematic review and meta-analysis published by Wan et al. (2026) specifically compared the differences between oliceridine and sufentanil regarding postoperative nausea and vomiting, providing high-level evidence-based support for clinical decision-making [12]. Furthermore, an exploratory analysis by Hammer et al. (2021) of two Phase III randomized, placebo- and active-controlled trials showed that, under conditions of equivalent analgesia, oliceridine was better tolerated than morphine [3].

Oliceridine Shows Broad Application Prospects in the Field of Procedural Sedation:

A single-center, randomized, parallel-group clinical trial conducted by Hu et al. (2026) evaluated the safety and efficacy of oliceridine combined with propofol for painless gastroscopy [13]. Yang et al. (2025) determined the half-effective dose (ED50) of oliceridine combined with remazolam for suppressing the intubation reaction during gastroscopy in adults. The results showed that oliceridine (13.19-14.46 μg/kg) combined with propofol demonstrated good safety and efficacy for painless gastroscopy, with a low incidence of complications [6]. A single-center, randomized controlled trial by Ma et al. (2025) compared the safety and efficacy of oliceridine and sufentanil in digestive endoscopy; the results showed that the sedation success rate was close to 100% in both groups, with oliceridine demonstrating an advantage in reducing adverse reactions [5].

This study used a base sedation regimen of remazolam combined with etomidate, to which either oliceridine or sufentanil was added. A randomized, double-blind, controlled trial conducted by Wang et al. (2026) in patients undergoing outpatient hysteroscopic polypectomy confirmed that the CRS scores in the oliceridine group at 5, 10, and 15 minutes post-awakening were significantly higher than those in the fentanyl and sufentanil groups (overall p-values of 0.002, 0.009, and <0.001, respectively). A multicenter randomized clinical trial by Hu et al. (2026) investigated the multimodal conscious sedation effects of oliceridine combined with alfentanil and local anesthesia in reconstructive upper blepharoplasty [7]. Patients in the group receiving multimodal intravenous sedation and analgesia with oliceridine and alfentanil combined with local anesthesia had significantly lower pain scores at all perioperative time points compared with the control group ($P < 0.05$), and the incidence of reflex tearing was significantly lower than that in the control group (6.9% vs. 75.0%, $P < 0.001$). Oliceridine demonstrates good efficacy and safety in such outpatient procedures [14].

Special Clinical Scenarios:

Prevention of Etomidate-Induced Myoclonus:

Etomidate is widely used for general anesthesia induction due to its hemodynamic stability, but the myoclonus it induces has long been a clinical challenge. A proof-of-concept randomized trial by Guo et al. (2026) found that premedication with oliceridine (0.03 mg/kg) significantly reduced the incidence of etomidate-induced myoclonus [15]. A prospective, randomized, double-blind, controlled study by Sun et al. (2026) further validated this finding, suggesting that oliceridine could serve as a novel premedication strategy for etomidate-induced anesthesia [12].

Safety and Adverse Reactions

Postoperative Nausea and Vomiting (PONV):

PONV is the most closely monitored safety endpoint in clinical studies of oliceridine. Multiple studies have shown that oliceridine is superior to sufentanil in reducing the incidence of PONV [2,4,8,9]. A meta-analysis by Wan et al. (2026) systematically compared the effects of the two agents on PONV; the pooled analysis showed that oliceridine significantly reduced the incidence of postoperative nausea (relative risk [RR] = 0.80, 95% CI: 0.70-0.90) [17]. Regarding respiratory depression, the incidence in the oliceridine group was 14.1%, significantly lower than the 21.8% observed in the sufentanil group (OR = 0.59, 95% CI: 0.39-0.90, P = 0.013) [5]. A study by Heng et al. (2026) further confirmed that, in patients at high risk for PONV, oliceridine also demonstrated a clinical advantage in reducing PONV [16].

Safety Comparison with Conventional Opioids:

Oliceridine demonstrated better tolerability than conventional opioids across all dose levels [3]. An exploratory analysis of a Phase III randomized, placebo- and active-controlled trial showed that, under conditions of equivalent analgesia, oliceridine was better tolerated than morphine [3]. Its adverse reaction profile consisted primarily of nausea, vomiting, dizziness, pruritus, and hypoxemia, but the overall incidence was lower than that of conventional opioids [3,17].

Safety in Special Populations:

Since the metabolites of oliceridine are inactive, it can be safely used in patients with impaired hepatic or renal function [1]. Oliceridine also demonstrates a favorable safety profile in elderly patients [2,16].

Outstanding Issues and Research Prospects

Although a substantial body of clinical evidence has accumulated for oliceridine, the following key issues still require further exploration.

Further Optimization of the Optimal Dose:

The effective dose of oliceridine varies across different clinical settings. Although Yang et al. (2025) determined the ED50 [6] of oliceridine in combination with remazolam for gastroscopy-induced reactions, the optimal dose for other types of surgery, such as laparoscopic surgery and open thoracic surgery, and under different combination regimens still requires validation through large-scale studies. Currently, there is significant variation in oliceridine administration regimens across studies, including loading dose, maintenance dose, and timing of administration, and there is an urgent need to establish a standardized perioperative treatment regimen.

Long-Term Safety and Use in Chronic Pain:

To date, research on oliceridine has almost exclusively focused on its short-term use for acute pain, ranging from several hours to several days [1-7,9-17]. There are currently insufficient data to determine whether its long-term use leads to tolerance, dependence, or hyperalgesia similar to those associated with traditional opioid medications. Furthermore, the potential role of oliceridine in managing chronic pain or cancer pain remains an area worthy of further exploration.

Comprehensive Impact on the Quality of Postoperative Recovery:

Most existing studies have used PONV as the primary endpoint, resulting in a relatively narrow assessment of the quality of postoperative recovery [17]. Although some studies have employed recovery quality scales, such as QoR-15 or QoR-40 [8,9], a more systematic evaluation is still needed regarding the drug's impact on clinical endpoints such as early postoperative ambulation, bowel function recovery, length of hospital stay, and patient satisfaction.

Heterogeneity Across Surgical Types and Patient Populations:

Current research is primarily concentrated in the fields of thoracic surgery [2,8], breast surgery [4], cholecystectomy [9], and endoscopy [5,13]; evidence remains very limited for surgeries in orthopedics, obstetrics and gynecology, neurosurgery, and cardiac surgery. Furthermore, data are particularly scarce for children, pregnant women, obese patients, and critically ill patients classified as American Society of Anesthesiologists (ASA) Class III or higher.

Optimal Positioning in Multimodal Analgesia:

The optimal role of oliceridine in the multimodal analgesia regimen of Enhanced Recovery After Surgery (ERAS) remains unclear. Its combination with regional anesthesia, nonsteroidal anti-inflammatory drugs (NSAIDs), acetaminophen, and other opioid medications urgently requires further research for optimization [7]. In addition, the combination of oliceridine with newer sedatives, such as remazolam, requires further validation.

Cost-Effectiveness Analysis:

As a new patented drug, the price of oliceridine is higher than that of traditional opioids. Against the backdrop of healthcare cost containment and diagnosis-related group (DRG) reimbursement, whether its clinical advantages, such as a reduction in PONV and a shorter post-anesthesia care unit (PACU) stay, can translate into economic benefits requires a pharmacoeconomic evaluation based on the Chinese population.

Conclusion

As the first approved G protein-biased μ-opioid receptor agonist, oliceridine, through its innovative biased signal transduction mechanism, significantly reduces the incidence of opioid-related adverse reactions, such as postoperative nausea and vomiting (PONV) and respiratory depression, while maintaining reliable analgesic efficacy [1,3,17]. Current evidence indicates that, in various perioperative settings, including thoracoscopic surgery, laparoscopic surgery, painless endoscopy, and outpatient surgery, oliceridine is at least as effective and safe as sufentanil and, in some cases, even superior [5,9]. However, issues such as the standardization of optimal dosing, safety during long-term use, applicability across different surgical procedures and special patient populations, and pharmacoeconomic value still require resolution through studies with larger sample sizes, longer follow-up periods, and higher quality. Future research should further clarify the optimal role of oliceridine in multimodal analgesia and ERAS protocols to promote its standardized application in clinical anesthesia and acute pain management.

Conflict of Interest

The author has read and approved the final version of the manuscript. The author declares no conflicts of interest.

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