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ORIGINAL RESEARCH

Oliceridine to prevent postoperative nausea and vomiting in high-risk patients undergoing general anaesthesia: a study protocol for a double-blind, randomised, controlled trial

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Abstract

Background: Postoperative nausea and vomiting (PONV) are distressing symptoms that considerably diminish postoperative satisfaction. We are conducting a double-blind, randomised, controlled trial to evaluate the efficacy of a novel G-protein-biased μ-opioid receptor agonist, oliceridine, in preventing PONV after general anaesthesia in high-risk patients. The study also seeks to determine whether traditional opioids, such as fentanyl, can be replaced during tracheal intubation and for postoperative analgesia. The objectives of this trial include assessing the impact of oliceridine on PONV. **Methods**: In this study, 280 adult female patients (aged 18–65 years) undergoing elective laparoscopic gynaecological under general surgery who meet the inclusion criteria will be randomly assigned to an experimental group (oliceridine) and a control group (fentanyl) in a 1:1 ratio. The primary outcome indicator is the incidence of nausea and vomiting within 48 hours after surgery. The secondary outcome indicators are the analgesic effect in the perioperative period (anaesthesia induction period, intraoperative period, and 48 hours post-surgery), the overall incidence of severe complications post-surgery, length of hospital stay, and time of food and drink intake. **Conclusions**: This trial demonstrates that oliceridine provides comparable analgesia to fentanyl in high-risk surgical patients, positioning it as a promising alternative with a superior PONV profile. **Clinical Trial Registration**: ChiCTR2400089121.

Keywords

Oliceridine fumarate injection; Postoperative nausea and vomiting; General anaesthesia; Fentanyl

1. Introduction

Postoperative nausea and vomiting (PONV) refer to feelings of nausea and episodes of vomiting that occur within 48 hours after surgery [1]. PONV is a distressing experience that significantly reduces postoperative patient satisfaction. Severe instances of PONV can lead to complications, such as tachycardia, increased salivation, and electrolyte imbalance, which may result in wound rupture, incisional hernia, aspiration pneumonia, prolonged hospital stays and increased medical costs [2]. The overall incidence of PONV in surgical patients is approximately 30%, although it can rise to 80% in the high-risk group. Recent guidelines reconfirm the various independent risk factors for PONV by performing multivariate data analyses on a broad cohort of patients. For adults, specific risk factors include being female, having a history of PONV or motion sickness, being a nonsmoker, and being under 50 [3]. Certain surgical procedures, such as laparoscopic surgery, bariatric surgery, gynaecological surgery, and cholecystectomy, are associated with an elevated risk of PONV. Additionally, anaesthetic factors, including the intraoperative use of volatile anaesthetics or nitrous oxide and postoperative use of opioids, also contribute to a heightened risk of PONV. A simple PONV risk-rating table for adults is presented in Table 1 [4].

Opioids stimulate μ-opioid receptors in the chemoreceptor trigger zone and cholinergic receptors in the vestibular system, resulting in nausea and vomiting by acting on the vomiting centre or via the afferent vagus and parasympathetic nerves. Different opioids possess varying affinities for different opioid receptors. While opioids primarily activate μ-opioid receptors of central nervous system may mediate nausea and vomiting, they can also activate κ-opioid and δ-opioid receptor subtypes in the gastrointestinal (GI) tract [5]. This activation affects GI functions by increased postprandial gastric accommodation and delayed gastric emptying, intestinal peristalsis, and

TABLE 1. A simple PONV risk rating table for adults.

Risk factor	Point per risk factor	Number of risk factors	Risk for PONV (%)
None		0	10
Female sex	1	1	20
History of PONV/motion sickness	1	2	40
Non-smoker	1	3	60
Expected postoperative opioids	1	4	80

Note: PONV, postoperative nausea and vomiting.

secretions, which can induce nausea and vomiting [6]. Despite their adverse effects, opioids play a vital role in perioperative analgesia. Consequently, developing new medications that maintain analgesic efficacy while reducing adverse effects could significantly improve patient safety.

Research into opioid mechanisms has revealed that traditional opioid agonists produce analgesic effects primarily by binding to μ-opioid receptors and activating G-protein-coupled receptors through various cellular signalling pathways. However, opioid agonists also bind to κ-opioid receptors, thereby activating the β-arrestin pathway, leading to adverse effects, such as respiratory and GI complications [7]. Research in β-arrestin knockout animals has demonstrated that morphine administration induces enhanced analgesia accompanied by decreased respiratory depression and constipation when compared with wild-type counterparts [8]. This indicates that the G-protein signalling pathway mainly mediates the analgesic effects of opioids, while the β-arrestin pathway is associated with adverse effects. By selectively administering G-protein-biased agonists, it may be possible to achieve effective pain relief while minimising the risk of adverse events [9]. Oliceridine, a newly approved intravenous opioid, acts as a G-protein-biased agonist of the μ-opioid receptor. It selectively activates the G-protein signalling pathway, significantly reducing the activation of the β-arrestin pathway, eventually decreasing the likelihood of opioid-related adverse effects while preserving analgesic efficacy. For patients at a high risk of PONV, oliceridine may present advantages over traditional opioids. However, further large-scale randomised controlled trials (RCTs) are needed to provide more compelling evidence to support these findings.

Oliceridine (Olinvyk®; TAG25C03, Trevena, Chester, PA, USA) was approved by the U.S. Food and Drug Administration in August 2020 and marketed as Oliceridine fumarate. By selectively targeting the G-protein sub-pathway instead of the β-arrestin pathway, oliceridine mitigates adverse effects, such as addiction, respiratory depression, and GI disturbances, while maintaining its analgesic effect [10]. A meta-analysis of six RCTs, including two that compared the effects of oliceridine and hydromorphone on PONV in orthopaedic patients, demonstrated that oliceridine significantly reduced the incidence of PONV and the need for antiemetic drugs [11].

To advance the knowledge in this field, this study will explore the effects of oliceridine on PONV in high-risk patients undergoing general anaesthesia, with the objective of improving their postoperative outcomes and quality of life.

2. Materials and methods

2.1 Research purpose

This study seeks to evaluate the effects of oliceridine, a G-protein-biased μ-opioid receptor agonist, on PONV in patients at high risk who are undergoing general anaesthesia. Additionally, it aims to assess the impact of oliceridine on perioperative analgesia (including anaesthesia induction, intraoperative care, and recovery within the first 48 hours post-surgery). The study will also investigate postoperative outcomes, such as the overall incidence of serious complications, length of hospital stay, and the timing of food and fluid intake. Furthermore, it will explore the potential to replace traditional opioids, such as fentanyl, during the tracheal intubation phase of anaesthesia. We anticipate that the findings will provide relevant theoretical guidance for managing perioperative analgesia and PONV in these patients.

2.2 Participants

The study will involve 280 female patients undergoing elective laparoscopic cholecystectomy or laparoscopic uterine and ovarian surgery who meet the criteria for sodium drainage. Participants will first be categorised by their surgical method and then randomly assigned to either the experimental group (oliceridine) or the control group (fentanyl) in a 1:1 ratio.

2.2.1 Inclusion criteria

1. Female patients with a simple adult PONV risk score $\geq$3 undergoing elective laparoscopic cholecystectomy or laparoscopic uterine and ovarian surgery under general anaesthesia.
2. American Society of Anaesthesiologists (ASA) grade I to III.
3. Body mass index of 18.5 to 29.9 kg/m^2.
4. Willing to provide informed consent.

2.2.2 Exclusion criteria

1. History of surgical operations under general anaesthesia within one month before the study.
2. Serious systemic cardiopulmonary or neurological diseases existing before surgery, including severe hypertension (crisis); severe diabetes (ketosis or acidosis); coronary heart disease; chronic obstructive pulmonary disease; asthma; respiratory failure; pulmonary hypertension; severe arrhythmias (*e.g.*, atrial fibrillation, Grade II or higher atrioventricular block, sick sinus syndrome); severe heart valve disease; heart failure, kidney failure, stroke, or myocardial infarction within

the last 6 months; Alzheimer's disease; Parkinson's disease; mental illness; obstructive sleep apnoea syndrome; or myasthenia gravis.

3. History of chronic pain.
4. Liver and kidney dysfunction, or leukopenia.
5. History of allergy to the drugs used in this study.
6. History of inflammatory bowel disease or peptic ulcer.
7. Abnormal coagulation function.
8. Patients with cancer undergoing radiotherapy or chemotherapy.
9. Patients who refused or were unable to cooperate with the study.
10. History of substance abuse.
11. Pregnancy.
12. Patients enrolled in other studies within the past 10 to 30 days.

2.2.3 Withdrawal criteria

Participants who withdraw from the study for any reason will be allowed, which may include but is not limited to:

1. The participant may withdraw their informed consent, leading to the termination of the study by the sponsor.
2. Serious AEs (Adverse Events) affecting the participant's continued participation.
3. Significant protocol violations or deviations.
4. Pregnancy.
5. Poor compliance.
6. Loss of follow-up.
7. The investigator or sponsor considers that the participant's medical condition may jeopardise their safety or that continued participation would harm their health.
8. Death.

2.2.4 Termination criteria

1. Serious safety issues occurring during the trial.
2. Major errors identified in the clinical trial protocol.
3. Termination of the study by the sponsor.
4. Termination requested by the Ethics Committee.

2.3 Trial design

Patients will be divided into two groups based on the surgical method: gallbladder operation group and gynaecological operation group. Subsequently, each group will be randomly assigned to either the experimental group (oliceridine group) or the control group (fentanyl group) at a 1:1 ratio using a random number table, with each group consisting of 70 patients. In addition to the different analgesics, both groups will follow the same protocols for anaesthesia induction, bilateral abdominal transverse fascia block, maintenance, and postoperative pain control. A dedicated staff, blinded to the patients' group assignment, will follow up with patients at 24- and 48-hours post-surgery and before discharge. Fig. 1 presents a flowchart of the experimental design.

2.4 Blind study

This study will implement a double-blind methodology, ensuring that participants are not involved in any other aspects of the research. According to the instructions for oliceridine use, a fentanyl dose of 0.05 mg is equipotent to oliceridine at a dose of 1 mg. Oliceridine and fentanyl concentrations were maintained at 1 mg/mL and 0.05 mg/mL, respectively, to ensure strict blinding to the analgesic drugs during the operation. Researchers responsible for recruitment and preoperative and post-operative follow-ups will be unaware of the group assignments. Fig. 2 illustrates the blinding methods that will be implemented in this study. Table 2 presents a comparison of the analgesic intensities of fentanyl and oliceridine.

2.5 Anaesthesia management

Preoperative assessment: Demographic data, allergy history, anaesthesia history, current medication history, ASA classification, routine blood tests, blood coagulation, blood biochemistry, and electrocardiograms of the participants included in the experiment will be recorded.

Pre-anaesthesia preparation: immediate and appropriate measures must be taken to ensure the participant's safety. Such events must be reported. Peripheral venous access will be established with a 16G intravenous catheter, and 0.9% normal saline will be infused. The anesthesiologist will determine the infusion rate and volume based on the patient's condition and a target-oriented fluid management strategy.

Anaesthesia induction: After completing full denitrogenation and oxygen administration, all patients will be administered fentanyl (0.15 mg) or oliceridine (3 mg), propofol (1.5–2.5 mg/kg), midazolam 0.02–0.05 mg/kg, and cisatracurium (0.15 mg/kg). Intubation will be performed 5 minutes after induction. Following induction, 0.375% ropivacaine (40 mL) will be administered for bilateral abdominal transverse fascial block.

Anaesthesia maintenance: During the maintenance phase, sevoflurane will be administered at 0.8–1.2 MAC. Cisatracurium will be continuously maintained at 6 mg/h, while either fentanyl (0.05 mg) or oliceridine (1 mg) will be administered according to hemodynamic changes. Urapidil will be administered if the systolic blood pressure increases by more than 30% of the baseline and persists for more than 5 minutes. If the systolic blood pressure falls below 30% of the baseline and persists for more than 5 minutes, ephedrine will be administered. The electroencephalogram (EEG) bi-spectral index (BIS) will be used to monitor the depth of anaesthesia during surgery; the BIS will be maintained at 40–55.

Anaesthesia recovery: Following surgery, the medical team will confirm that the patient is conscious and able to breathe, with complete restoration of throat function, swallowing capabilities, and cough reflexes. The tracheal tube will be removed once normal tidal volume and minute ventilation have been established. Patients with a steward score greater than four will be transferred to the post-anaesthesia care unit (PACU). Oxygen will be administered through a nasal cannula, and an electrocardiogram, blood oxygen, and blood pressure will be monitored for 30 minutes. The patient will return to the ward if the Aldrete recovery score remains above 9.

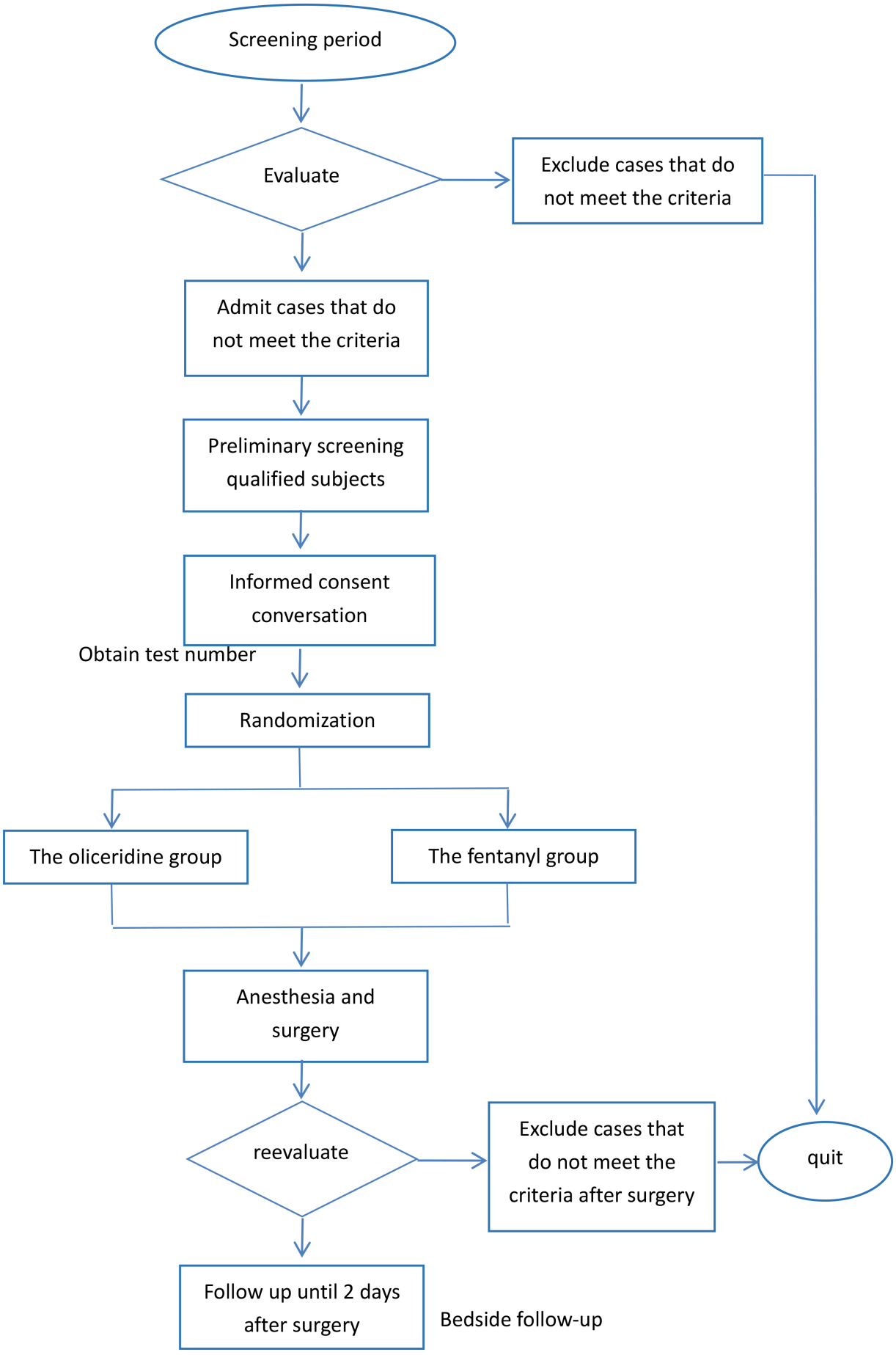

FIGURE 1. Flowchart of the trial design.

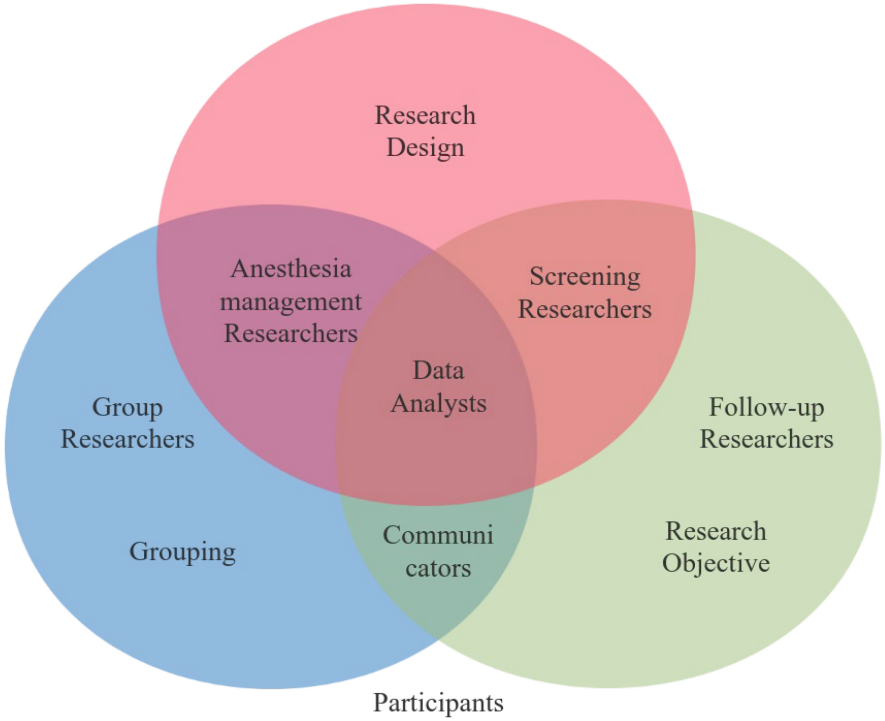

FIGURE 2. Diagram showing the study blinding method.

TABLE 2. Comparison of analgesic intensity between fentanyl and Oliceridine.

Restoratives	Fentanyl	Oliceridine
Analgesia level	Potent	Intermediate
Analgesic intensity	80–100	3–5
Onset time	1–2 min	2–5 min (median 1–3 min)
Peak time	3–6 min	5–15 min
Half-life period	20 min	1.3–3 h
Metabolite	Inactivity Obvious accumulation	Inactivity Acusis
Nausea and vomiting	Obvious	Mild
Respiratory depression	Obvious	Mild
Cyclic inhibition	Obvious	Mild
Effects on liver function	Influential	Minimal
Effects on renal function	Influential	Minimal
Addiction	High	Low

2.6 Postoperative analgesia and PONV management

Performing a nerve block for perioperative analgesia can effectively alleviate perioperative pain, ultimately benefiting patients. As an essential component of perioperative multimodal analgesia, a total of 40 mL of 0.375% ropivacaine will be administered with bilateral transverse abdominal fascia block for postoperative analgesia. Patients will be routinely administered 30 mg of ketorolac acid intramuscularly, once daily, post-surgery. If patients report a visual analogue scale (VAS) score greater than 3 in the PACU or within 48 hours after surgery, 30 mg of ketorolac will be administered as needed. Follow-up staff will monitor patients at 24- and 48-hours post-surgery and before discharge. In instances where patients have pre-existing PONV, we will conduct timely resuscitation treatment. If patients experience nausea and vomiting with a VAS score greater than 3, 10 mg of metoclopramide and 10 mg of dexamethasone will be administered and recorded. Dexamethasone is widely recognised as an effective medication for managing postoperative vomiting [12]. Research shows a higher dose of dexamethasone may confer greater and more prolonged protection against PONV [13]. Furthermore, intravenous dexamethasone serves as an adjuvant analgesic that can enhance pain relief, also in a dose-dependent manner [14]. In our trial, a nerve block will be used for postoperative

analgesia. Therefore, considering the comfort and safety of patients comprehensively, we set the dexamethasone dosage at 10 mg.

2.7 Follow-up period

Full-time staff will monitor patients 24 and 48 hours after surgery and prior to discharge. The overall incidence of PONV will be assessed within 48 hours post-surgery.

2.8 Outcomes

2.8.1 Primary outcome measure

The incidence of nausea and vomiting will be evaluated 48 hours after surgery. Trained anaesthesia nurses who are blinded to the group allocation will collect statistical data, general clinical features, and information on PONV at 24- and 48-hours post-surgery. They will also follow up with the patients. The incidence of nausea and vomiting will be monitored at two different time periods: 24 hours after surgery and 24 to 48 hours after surgery. The incidence of nausea and vomiting in each time period will be recorded. If nausea and vomiting occur, it will be recorded as "1"; if no nausea and vomiting occur, it will be recorded as "0".

2.8.2 Secondary outcome measure

The severity of nausea and vomiting 48 hours post-surgery will be evaluated using a VAS score [15]. Additionally, the recovery rate, the number of additional analgesic drugs used, and the total amount of analgesic drugs administered will be recorded. The severity of PONV will be monitored, and instances of nausea and vomiting in the PACU will be recorded 24 hours after surgery and 24 to 48 hours after surgery. In cases of vomiting, a single dose of 10 mg of metoclopramide and 10 mg of dexamethasone will be administered and noted as "1" on the postoperative record sheet. The frequency and dosage of the drug will also be recorded.

Hemodynamic parameters will be recorded at each time point: before anaesthesia induction (T1), immediately after intubation (T2), at incision (T3), 5 minutes after extubation (T4), and at the time of discharge (T5). The number and total amount of postoperative non-steroidal anti-inflammatory drugs administered will also be recorded. VAS scores for resting pain and motor pain will be assessed at 24- and 48-hours post-surgery and at each time point prior to discharge. The recovery time of intestinal exhaust, water drinking, eating, mobilisation, drainage tube removal, and hospitalisation will be noted. Intraoperative and postoperative complications, including hypersensitivity, arrhythmia, acute myocardial infarction, cardiac arrest, hypotension, delayed recovery, respiratory depression, and other serious complications, will be recorded.

2.9 Statistical analysis

Statistical analysis will be performed using IBM SPSS Statistics 20 (IBM Corp., Armonk, NY, USA). Normally distributed data will be presented as the mean $\pm$ standard deviation, while non-normally distributed data will be reported as the median and interquartile range. Count data will be expressed as percentages (%), with group comparisons performed using the chi-square (χ^2) test. Measurement data will be analysed using the *t*-test or Mann-Whitney U test. Statistical significance will be set at $p < 0.05$.

2.10 Sample size calculation

According to literature, although the overall incidence of PONV in patients undergoing surgery is 30%, it can reach 80% in high-risk groups [16–18]. In the intervention group, the odds ratio (OR) was calculated at 3.14, with an alpha (α) of 0.05 and a beta (β) of 0.2. The *z*-score for alpha (μ_alpha) was 1.96, while the *z*-score for beta (μ_beta) was 0.84. Consequently, the required number of effective cases per group was determined to be 63. Considering a 10% anticipated loss to follow-up, the number of valid cases per group was increased to 70. The study will employ a stratified randomisation design based on the surgical method, leading to a total required sample size of 140 cases for laparoscopic cholecystectomy and 140 cases for laparoscopic uterine and ovarian surgery.

2.11 Data management

Participant data on the case report form should be recorded using a participant code; the participant can be identified by this code or initials.

The investigator must collect all participant data as specified by the protocol and record it in the original medical records.

The investigator or authorised research centre staff will enter study data into the electronic Case Report Form (eCRF).

All data entered into the eCRF should be in simplified Chinese and must be completed during or immediately after the visit. The investigator must review the data to ensure accuracy and correctness.

An auditor will evaluate the eCRFs for completeness and consistency and compare them with the original documents to ensure the consistency of key data. The investigator or designee will be responsible for recording, correcting, and modifying all data; the monitor will not have this authority. If any data discrepancies arise, the auditor or data manager will raise the issue, and the research centre staff will respond accordingly.

Unless otherwise specified, the eCRF will be solely used for data collection and will not be considered source material. Original documentation encompasses all records used by the investigator or research centre relevant to the participants, demonstrating the participants' existence, inclusion criteria, and study participation.

The investigator will maintain all original documents and ensure they are monitored at every visit. Additionally, the investigator must submit a complete eCRF for each participant, regardless of the duration of study participation. All supporting documents submitted with the eCRF should be carefully verified for study numbers and random participant numbers. Furthermore, all personal privacy information (including participant names) should be removed or rendered illegible to protect the participants' privacy.

2.12 Quality control of this study

Clinical study participants will receive standardised training in the field to ensure consistency in the quality of multicentre studies. Researchers must record the contents of the forms truthfully and accurately, thereby ensuring the reliability of the research medical records. All observations and laboratory data in clinical studies must be verified to ensure data reliability, guaranteeing that conclusions are drawn from the original and reliable data. Every three months from the start of the study, we will hold discussions to address any challenges encountered during the research process to ensure consistent implementation of the procedures. The investigator will be required to adhere to the clinical study protocol strictly and will not make unauthorised modifications during the study period. If revisions are necessary, the applicant and researcher must discuss and decide on them together. Revised clinical study protocols must be addressed and approved by the Ethics Committee.

2.13 Safety evaluation of this study

All AEs occurring between the signing of informed consent and the administration of the investigational drug will be systematically recorded in the eCRF. Each entry shall provide a detailed description of the AE, including any associated symptoms, time of occurrence, severity, duration, correlation with the investigational drug, action taken, and outcome. In cases of serious AEs, immediate and appropriate measures must be taken to ensure the participant's safety. Such events must be reported within 24 hours to the relevant authorities, including the drug registration applicant, the State Drug Administration, the provincial Food and Drug Administration, the ethics committee of the clinical trial centre, the Medical Department of the Medical Administration Bureau of the Health Commission, and the ethics committee of the group leader. If any participant experiences harm while participating in this study, they will receive timely treatment and compensation in accordance with applicable laws and regulations.

2.14 Recruitment of participants for this study

Physicians and researchers from Dongtai People's Hospital will recruit participants for this study.

2.15 Rights and interests of participants in this study

1. Acquisition of informed consent: This study fully adheres to the principles of volatilisation. Prior to inclusion, written informed consent will be obtained from the participants and their legal representatives. Participants have the right to withdraw from the study at any time.

2. Benefits: The results of this study will provide a theoretical basis for future research. Participants will receive appropriate medical care and protection throughout the study.

3. Compensation: This study does not cover transportation expenses, compensation fees, or nutrition fees for participants.

4. Medical treatment and protection of participants: Throughout the study, participants will receive medical treatment and protection related to clinical diagnosis and treatment.

2.16 Participant privacy and confidentiality

Throughout this study, the researcher will ensure the privacy and confidentiality of the participant's personal information. Without proper authorisation, the researcher will not disclose personal information to a third party.

2.17 Patients and public involvement

The patients and the public were not involved in the design, conduct, reporting, or dissemination of our research, and no attempt will be made to assess the burden of the intervention on the patients themselves.

2.18 Side effects of oliceridine

1. Addiction, abuse, and misuse.
2. Life-threatening respiratory suppression.
3. Neonatal opioid withdrawal syndrome.
4. Interaction with benzodiazepines or other CNS (Central Nervous System) inhibitors.
5. Adrenal gland hypofunction.
6. Severe hypotension.
7. Gastrointestinal adverse events.
8. Epilepsy.
9. Withdrawal response.

3. Strengths and limitations of this study

1. This double-blind, randomised, controlled trial will be the first to evaluate the effect of oliceridine on postoperative nausea and vomiting (PONV) in high-risk patients undergoing general anaesthesia.

2. As all participants will be female, randomisation was employed to assign patients to either the oliceridine or fentanyl group in a 1:1 ratio, with numbers ranging from smallest to largest.

3. Full-time staff, who were blinded to the patients' group assignment, followed up with the patients 24 and 48 hours after surgery, and before discharge.

4. Although this study will include 280 patients, the sample size might not be large enough; more randomised controlled trials are needed.

5. The trial will not follow up with the patients for a long time, only 48 hours after surgery; some patients may experience delayed PONV and other adverse effects.

6. The various scoring scales used in this experiment, such as the visual analogue scale (VAS), have a certain degree of subjectivity, and avoiding the existence of error indicators may be difficult.

7. The types of surgeries in this study will be relatively short, the use of opioids will be minimised, and there will be no surgeries with complex or long operation times, including cardiac or hepatobiliary surgeries. Whether oliceridine can effectively prevent the incidence of PONV with complex surgery and long operation time is worthy of further exploration.

8. The market duration of oliceridine used in this trial is relatively short, and the mechanism of action for this drug needs further improvement. Additionally, the lack of safety evidence from experiments in certain special groups limits the widespread application of oliceridine.

4. Conclusions

This double-blind, randomized controlled trial demonstrates that oliceridine, a novel G protein-biased μ-opioid receptor agonist, provides comparable analgesic efficacy to fentanyl during the induction, intraoperative, and recovery phases of perioperative care in high-risk patients under general anesthesia, while serving as a promising and viable alternative with a particular advantage in reducing postoperative nausea and vomiting (PONV). Additional studies in larger, more diverse cohorts should be conducted to validate these findings.

ABBREVIATIONS

AEs, adverse events; ASA, American Society of Anesthesiologists; BIS, bi-spectral index; eCRF, electronic Case Report Form; EEG, electroencephalogram; GI, gastrointestinal; OR, odds ratio; PACU, post-anaesthesia care unit; PONV, postoperative nausea and vomiting; RCT, randomised controlled trial; T1, before anaesthesia induction; T2, immediately after intubation; T3, at incision; T4, 5 minutes after extubation; T5, at discharge; VAS, visual analogue scale; CNS, Central Nervous System.

AVAILABILITY OF DATA AND MATERIALS

Data sharing is not applicable to this article, as no datasets were generated or analyzed during the current study.

AUTHOR CONTRIBUTIONS

ZX—initially formulated the research ideas. AX—wrote the manuscript, completed the ethical approval and trial registration processes. SC—will perform the preoperative interview and grouping. XH and CC—will collect and store all data from this trial. YX—will perform fascia iliac block. RD—will be responsible for the postoperative follow-up work, including the evaluation of PONV and pain. JZ—calculated the sample size and will be responsible for data analysis. All authors contributed to the design of trial protocols.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

This study protocol adheres to the Declaration of Helsinki requirements. The study protocol was approved by the Ethics Committee of Dongtai People's Hospital (20240820). Any modifications to the protocol will be made only after submission to the Ethics Committee, and the study will be suspended until the Ethics Committee grants approval. This trial is registered with the Chinese Clinical Trial Registration Centre under the registration number ChiCTR2400089121. The original data are anticipated to be released in January 2027 on the ResMan original data-sharing platform (IPD-sharing platform) of the China Clinical Trial Registry, accessible at http://www.medresman.org.cn. Informed consent to participate will be obtained from all participants.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

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