

Effects of Oliceridine versus Sufentanil on Postoperative Recovery Quality during Hysteroscopy under Laryngeal Mask Airway Anesthesia: Protocol for a Single-Blind and Randomized Controlled Trial

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Effects of Oliceridine versus Sufentanil on Postoperative Recovery Quality during Hysteroscopy under Laryngeal Mask Airway Anesthesia: Protocol for a Single-Blind and Randomized Controlled Trial

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Abstract

Background: Hysteroscopy, the gold standard for diagnosing and treating intrauterine pathologies, shows substantial growth in clinical practice. Nevertheless, early postoperative pain and opioid-related adverse effects remain critical determinants of recovery quality. Oliceridine—a novel G protein-biased μ -opioid receptor agonist—demonstrates an improved therapeutic range over conventional opioids in preliminary studies. This trial aims to determine whether oliceridine enhances early recovery quality while reducing opioid-related complications compared to sufentanil in patients undergoing hysteroscopy under general anesthesia.

Objective: This study aims to evaluate whether oliceridine, compared with sufentanil, provides non-inferior intraoperative analgesia while demonstrating superior postoperative recovery quality and reduced opioid-related complications in patients undergoing hysteroscopy under general anesthesia.

Methods: This single-center randomized controlled trial will enroll 120 patients undergoing hysteroscopy under general anesthesia with 1:1 randomization to sufentanil- or oliceridine-based analgesia; the primary outcome is early recovery quality assessed by the QoR-15 scale at 24 hours postoperatively, while secondary outcomes include hemodynamic fluctuations during induction, total intraoperative opioid consumption and supplemental bolus frequency, proportion requiring vasoactive agents, incidence of respiratory depression in PACU, postoperative extubation time, opioid-related adverse events within 24 hours, and VAS pain scores at 30 minutes, 4 hours, 8 hours, and 24 hours post-extubation.

Results: This study received approval from the Medical Ethics Committee of Deyang People's Hospital on April 16, 2025 (approval no. 2025-03-009-K01). Participant recruitment is currently in progress and is anticipated to be completed by the end of 2025. Data analysis, manuscript preparation, and submission for publication are expected to take place throughout the first quarter of 2026.

Conclusions: This randomized controlled trial is designed to evaluate early recovery quality following hysteroscopy under general anesthesia. We aim to investigate whether oliceridine demonstrates an advantage over sufentanil in enhancing postoperative recovery while mitigating opioid-related adverse effects. Although conducted at a single center and lacking long-term perioperative safety data for oliceridine, this study will provide foundational evidence to inform future clinical investigations. Clinical Trial: This study was prospectively registered at the Chinese Clinical Trial Registry (Registration number: ChiCTR2500104024; Date: 10 Jun 2025).

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Title

Effects of Oliceridine versus Sufentanil on Postoperative Recovery Quality during Hysteroscopy under Laryngeal Mask Airway Anesthesia: Protocol for a Single-Blind and Randomized Controlled Trial

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Abstract

Background:

Hysteroscopy, the gold standard for diagnosing and treating intrauterine pathologies, shows substantial growth in clinical practice. Nevertheless, early postoperative pain and opioid-related adverse effects remain critical determinants of recovery quality. Oliceridine—a novel G protein-biased μ -opioid receptor agonist—demonstrates an improved therapeutic range over conventional opioids in preliminary studies. This trial aims to determine whether oliceridine enhances early recovery quality while reducing opioid-related complications compared to sufentanil in patients undergoing hysteroscopy under general anesthesia.

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Author details {5a}	1 Department of Anesthesiology, Deyang People's Hospital, Deyang 618000, China

	2 School of Medical and Life Sciences, Chengdu University of Traditional Chinese Medicine, Chengdu 611137, China Jia Han and Yu-Hang Shou conceptualized and designed the trial and drafted the initial protocol; Yu-Hang Shou prepared the preliminary manuscript; Jia Han and Xian-Jie Zhang finalized the manuscript; Jian-Sheng Luo and Wen-Hu Zhai were responsible for participant recruitment and allocation. All authors have read and approved the final manuscript.
Name and contact information for the trial sponsor {5b}	Jia Han, Department of Anesthesiology, Deyang People's Hospital, Deyang 618000, China. E-mail: will418@126.com.
Role of sponsor {5c}	The funding sources had no role in the design of this study and will not.

Keywords

Oliceridine, Hysteroscopy, Quality of Recovery, Opioid-Related Adverse Events

Introduction

Hysteroscopy is currently recognized as the gold standard for diagnosing and treating intrauterine pathologies, having revolutionized gynecological diagnostics and operative interventions. This modality enables both diagnostic evaluations and surgical treatments through a minimally invasive approach, characterized by rapid postoperative recovery. Advancements in hysteroscopic technologies and instrumentation have substantially increased its adoption across diverse patient populations [1, 2]. Pain remains a leading cause of procedural failure during hysteroscopy. To optimize surgical conditions and enhance satisfaction for both patients and surgeons, hysteroscopic procedures in China are predominantly performed under general anesthesia. A nationwide survey revealed that 63.8% of hysteroscopic surgeries utilized anesthesia in 2021, underscoring its critical role in contemporary practice [3]. European data corroborate this pattern, with a retrospective analysis confirming that a proportion of hysteroscopic procedures also necessitate general anesthesia for successful completion [4].

To date, no robust evidence exists to define optimal anesthesia protocols for pain management in hysteroscopy, and standardized approaches remain underexplored. For hysteroscopic procedures anticipated to be lengthy or involving significant tissue trauma, the 2020 Chinese Expert Consensus on Anesthesia Management recommends general anesthesia with laryngeal mask airway (LMA) to ensure procedural tolerance [5]. Current clinical practice predominantly utilizes conventional opioids like sufentanil for intraoperative analgesia. However, sufentanil administration is associated with multiple opioid-related adverse effects—including nausea, vomiting, excessive sedation, respiratory depression, drug tolerance, and opioid-induced hyperalgesia (OIH)—which collectively compromise early postoperative recovery [6].

Oliceridine is a novel G protein-biased μ -opioid receptor agonist that selectively activates G protein signaling while minimizing β -arrestin recruitment. This pharmacological profile confers a mechanistic advantage: selectively engaging intracellular analgesic pathways while avoiding those mediating adverse effects [7, 8]. As such, oliceridine has garnered emerging clinical interest for hysteroscopic analgesia.

The Quality of Recovery (QoR) is a multidimensional construct evaluating patient-centered recovery, encompassing physical, physiological, psychological, social, and functional domains [9, 10]. The QoR-15 scale—validated for reliability and clinical utility—quantifies recovery across five dimensions: physical comfort, emotional status, psychological support, independence, and pain experience. Postoperative pain intensity, nausea/vomiting incidence, and opioid consumption profiles constitute key determinants of patient recovery quality [11, 12].

Therefore, this study utilizes the QoR-15 scale as the primary endpoint to evaluate oliceridine's efficacy within LMA-based general anesthesia for hysteroscopy. We aim to determine whether oliceridine demonstrates superiority over sufentanil in enhancing early postoperative recovery quality while reducing opioid-related adverse events.

Methods

Study Design

This prospective, single-center, single-blind, randomized controlled study will be conducted

at the Gynecology and Pediatrics Hospital of Deyang People's Hospital. The protocol received ethical approval from the Institutional Ethics Committee (No. 2025-03-K01) and was registered at the Chinese Clinical Trial Registry. Written informed consent will be obtained from all participants or their legal guardians. Eligible patients will be randomly allocated to either the sufentanil (S) group or oliceridine (O) group. The participant timeline is shown in Fig. 1. A time schedule for enrollment, interventions, and assessments is detailed in Fig. 2.

Eligibility criteria

Inclusion criteria: (1) Patients scheduled for hysteroscopic surgery under laryngeal mask airway (LMA) general anesthesia who were assessed by physicians as unable to tolerate the pain stimuli associated with surgical manipulation. (2) Aged 18 to 65 years old. (3) American Society of Anesthesiologists (ASA) physical status I–III. (4) Voluntary signing of informed consent.

Exclusion criteria: (1) ASA physical status IV or higher (indicating severe systemic disease, functional incapacity, including but not limited to: NYHA class III or higher heart failure, myocardial ischemia, severe reduction in cardiac ejection fraction, third-degree atrioventricular block, stage 3 hypertension, respiratory failure, severe COPD, severe pulmonary dysfunction, or decompensated hepatic or renal insufficiency). (2) Known allergy to any component of the investigational drugs or contraindications to their use. (3) Inability to cooperate (e.g., psychiatric disorders, anticipated difficulty with neuropsychological assessment, or communication barriers due to pronunciation or dialect). (4) History of alcohol or substance abuse. (5) Concurrent participation or participation in another clinical trial within 12 weeks prior to this trial. (6) BMI > 30 kg/m². (7) Inability to comprehend the study procedures or refusal to participate. (8) Deemed unsuitable for participation by the investigator's assessment.

Who will take informed consent? {26a}

Eligible patients will undergo preoperative screening. Written informed consent will be obtained from all participants or their legal guardians prior to or on the day of surgery. We ensure comprehensive disclosure of potential benefits and risks, with full participant comprehension verified before consent signing.

Randomization and Blinding

Block randomization will be performed using a computer-generated sequence created via the randomization.com website. An independent researcher not involved in the trial will prepare sequentially numbered, opaque, sealed envelopes containing group assignments. Participants will be allocated in a 1:1 ratio to either the experimental or control group by opening these envelopes in sequential order at the time of enrollment. Allocation cards will be sealed inside opaque envelopes to ensure concealment. Blinding will be maintained for both participants and outcome assessors throughout the trial to minimize assessment bias. The blinding will be broken only in the event of severe adverse events.

Who will be blinded {17a}

Study participants, their legally authorized representatives, and outcome assessors were blinded to group allocation throughout the trial. The administering anesthesiologist performing intravenous drug delivery remained unblinded due to procedural requirements; however, this individual was excluded from all subsequent research activities.

Procedure for unblinding if needed {17b}

Unblinding the allocation is generally not required per protocol. Emergency unblinding will be performed exclusively to determine rescue medications for critical adverse events or during other medical emergencies

Interventions

Explanation for the choice of comparators {6b}

This study evaluates the impact of oliceridine (Group O) on early postoperative recovery quality in patients undergoing hysteroscopic surgery under general anesthesia. The sufentanil-based regimen (Group S) serves as the comparator, because its status as the conventional analgesic approach for such procedures in current clinical practice.

Both groups will receive identical anesthesia induction and maintenance protocols, but with divergent analgesic regimens. Group O will be administered oliceridine at a dose of 60 µg/kg (diluted to 10 mL with normal saline) as a slow intravenous bolus for induction. Supplemental doses of 30 µg/kg will be provided if intraoperative analgesia is deemed inadequate, defined as mean arterial pressure (MAP) and/or heart rate (HR) exceeding 20% above baseline values. Group S will receive sufentanil at a dose of 0.3 µg/kg (similarly diluted to 10 mL) as an induction bolus, with supplemental doses of 0.15 µg/kg

administered under the same hemodynamic criteria.

Anesthesia Protocol

Upon arrival in the operating room, standard monitoring—including pulse oximetry, invasive radial arterial blood pressure, and electrocardiography—will be initiated. Thirty minutes prior to induction, the attending anesthesiologist will administer intravenous penehyclidine hydrochloride (0.01 mg/kg) and ondansetron (4 mg). Anesthesia induction will begin with a slow intravenous bolus of either sufentanil or oliceridine according to group assignment. One minute later, propofol (2 mg/kg) and cisatracurium (0.15 mg/kg) will be administered. After satisfactory neuromuscular blockade is achieved, a laryngeal mask airway will be inserted. Mechanical ventilation will be initiated with a tidal volume of 6–8 mL/kg predicted body weight and PEEP of 5 cmH₂O. Anesthesia will be maintained using a continuous infusion of propofol (4–12 mg/kg/h), with supplemental opioids administered based on hemodynamic criteria (MAP or HR >20% above baseline). The propofol infusion rate will be titrated to maintain a BIS value between 40 and 60. Neuromuscular blockade will be maintained with intermittent boluses of cisatracurium (one-third of the induction dose). If reversal is required, neostigmine (0.02 mg/kg) and atropine (0.01 mg/kg) will be administered. After surgery, all patients will be transferred to the post-anesthesia care unit (PACU).

Criteria for discontinuing or modifying allocated interventions {11b}

The criteria for discontinuing are as follows

1. Severe anesthesia/surgical complications (e.g., anaphylaxis, shock, cardiac arrest, malignant arrhythmias, aspiration requiring intervention, malignant hyperthermia [MH]).
2. Protocol deviation in anesthesia/surgical technique.
3. Withdrawal of consent.
4. Anticipated difficult airway.
5. failed laryngeal mask airway (LMA) placement.

Strategies to improve adherence to interventions {11c}

The principal investigator conducted preoperative evaluations against inclusion/exclusion criteria one day prior to surgery. During informed consent, investigator detailed study procedures to participants and legally authorized representatives, outlining participant

responsibilities.

Relevant concomitant care permitted or prohibited during the trial {11d}

The provision of additional care during the trial followed institutional protocols.

Outcomes

The primary outcome is defined as the quality of postoperative recovery at 24 hours after surgery and will be assessed using the 15-item Quality of Recovery (QoR-15) scale (score range: 0-150; higher scores indicate better recovery). Secondary efficacy endpoints include: (1) hemodynamic changes during induction (HR/MAP at T0 [pre-drug], T1 [pre-LMA], T2 [post-LMA immediate], T3 [5-min post-LMA]); (2) total intraoperative opioid consumption and supplemental bolus frequency; (3) proportion requiring vasoactive agents; (4) incidence of PACU respiratory depression (defined as respiratory rate <6 bpm, ETCO₂ amplitude change >50 mmHg or <30 mmHg, or waveform loss >20s); (5) time to extubation; (6) opioid-related adverse events within 24h; and (7) VAS pain scores at 30 minutes, 4 hours, 8 hours, and 24 hours post-extubation.

Data Collection and Management

Baseline data will include demographic characteristics (age, sex, BMI) and comorbidities with diagnostic verification. Intraoperative records will include vital signs, anesthetic agents/dosages, surgical duration, and proportion requiring vasopressor administration. In the post-anesthesia care unit (PACU), time to extubation, early postoperative VAS pain scores, and incidence of respiratory depression will be documented. Postoperative recovery quality will be assessed at 24 hours using the QoR-15 scale, with 24-hour adverse events systematically recorded. Predefined subgroup analyses stratified by age will be conducted for primary and secondary outcomes, applying identical statistical approaches as specified for the main analyses.

Source data will be documented using standardized case report forms (CRFs). To minimize data entry errors, independent dual-entry verification will be performed. Physical records will be stored securely in locked cabinets with restricted access within the Department of Anesthesiology. Electronic data will be hosted on encrypted, cloud-based platforms.

Data Reporting Guidelines

The SPIRIT reporting guidelines will be used for this paper.

Sample Size

Based on clinical observations suggesting enhanced postoperative recovery in patients receiving oliceridine versus sufentanil during hysteroscopic surgery under laryngeal mask airway general anesthesia, we conducted a preliminary retrospective analysis of Quality of Recovery-15 (QoR-15) scores. In this pilot assessment of 20 patients (n=10 per group), the sufentanil group demonstrated a mean QoR-15 score of 129.8 ± 4.92 compared to 132.9 ± 6.25 in the oliceridine group. Subsequent sample size estimation was performed using G*Power 3.1 software. An independent samples t-test (Means: Difference between two independent means) with $\alpha=0.05$ (two-tailed) and 80% power indicated a minimum requirement of 106 participants. Accounting for an anticipated 10% attrition rate, a final cohort of 120 patients will be enrolled.

Recruitment Plan

Based on institutional surgical volume projections, patient recruitment is scheduled to commence in July 2025 and is anticipated to be completed within a five-month period to enroll the target cohort of 120 participants. Preoperative screening for eligible candidates will be conducted by the investigators. Written informed consent will be obtained from all participants or their legally authorized representatives either before or on the day of surgery. The consent process, approved by the institutional review board, ensures comprehensive disclosure of potential benefits, risks, and alternative treatments. Documentation will confirm that all participants have fully understood the information before providing their signature.

Statistical Analysis

Primary/secondary outcomes will be analyzed using SPSS Statistics v27.0, with continuous variables first assessed for normality via Kolmogorov-Smirnov (KS) testing; normally distributed data will be expressed as mean $\pm$ standard deviation (SD), non-normal data as median (interquartile range), and categorical variables as counts (percentages).

Quantitative between-group comparisons will employ independent-samples t-tests or Mann-

Whitney U tests, while qualitative comparisons will use chi-square, continuity-corrected chi-square, or Fisher's exact tests, with all tests being two-tailed (statistical significance threshold: $p < 0.05$).

Methods in analysis to handle protocol non-adherence and any statistical methods to handle missing data {20c}

Prior to enrollment, comprehensive study details will be disclosed to potential participants, with written informed consent obtained from patients and their legally authorized representatives. Investigators may discontinue participation for substantial protocol deviations (e.g., non-attendance at scheduled visits), initiating replacement recruitment according to randomization sequence.

Plans to promote participant retention and complete follow-up {18b}

Investigators will maintain ongoing communication with participants throughout the trial to address concerns while ensuring protocol adherence. Participant involvement may be discontinued by investigators in cases of non-adherence to scheduled visits or substantial protocol deviations, with all collected data excluded from final analysis per intention-to-treat principles.

Ethical Considerations

This study received approval from the Institutional Ethics Committee of Deyang People's Hospital (approval no. 2025-03-009-K01). All procedures strictly adhered to legislative and institutional requirements, with no involvement of vulnerable populations. Written informed consent will be obtained from every participant prior to enrollment.

Results

The first patient was enrolled on July 11, 2025. As of September 2025, a total of 55 participants have been enrolled out. Data analysis, manuscript preparation, and submission for publication are expected to take place throughout the first quarter of 2026.

Adverse event reporting and harms {22}

All AEs (including intraoperative hypertension, nausea/vomiting, respiratory depression,

dizziness, headache, and procedure-related complications) will be documented in case report forms (CRFs). Upon AE occurrence, immediate protective measures will be implemented to ensure participant safety. Events will be reported to the principal investigator (PI) for causality assessment and determination of study continuation. Serious/unexpected AEs undergo expedited reporting (within 24 hours) to the Institutional Ethics Committee.

Discussion

Anticipated Findings

Hysteroscopy serves as a minimally invasive modality for diagnosing and treating intrauterine pathologies, with indispensable roles in managing endometrial polyps, abnormal uterine bleeding, intrauterine adhesions, uterine septa, endometrial hyperplasia, and early-stage endometrial cancer [13-15]. Procedures requiring prolonged operative time or large instrumentation necessitate anesthesia in operating room settings[16]. In China, LMA-based general anesthesia is currently a prevalent approach for hysteroscopic surgery[17]. Conventional analgesic protocols predominantly utilize traditional opioids like sufentanil. However, these agents frequently induce respiratory/circulatory depression, nausea/vomiting, excessive sedation, immunosuppression, opioid-induced hyperalgesia, constipation, and abdominal distension[18-21]. Although effective for anesthesia, these complications prolong hospitalization, increase perioperative management complexity, and compromise postoperative recovery quality. Consequently, reducing opioid-related adverse events is crucial for enhancing recovery.

Oliceridine is a synthetic μ -opioid receptor agonist distinguished from conventional opioids by its G protein-biased selectivity, which mediates potent analgesia while substantially reducing β -arrestin recruitment—a signaling pathway strongly associated with opioid-related adverse events. In contrast, traditional opioids (e.g., morphine, fentanyl) non-selectively activate both G protein and β -arrestin pathways upon μ -receptor binding[22, 23]. Clinical trial evidence confirms that oliceridine significantly reduces nausea, vomiting, and respiratory complications compared to morphine [24-27]. Therefore, we postulate that this mechanistic advantage of oliceridine may similarly confer clinical benefits when compared with sufentanil.

The QoR-15 scale was selected to assess postoperative recovery quality as a validated patient-reported outcome measure evaluating five key recovery dimensions following anesthesia and surgery. Its established reliability and practical clinical utility underpin widespread adoption[11]. The Chinese version has been formally validated, demonstrating robust reliability, validity, and user-friendliness[28]. These properties support its extensive application in clinical trials for postoperative recovery assessment.

Limitations

No prior studies have established whether oliceridine's mechanistic advantages translate to enhanced recovery quality in hysteroscopic surgery under general anesthesia. But there are a number of potential limitations in the study design: (1) single-center design—though protocol standardization ensures internal validity, generalisability may be limited; (2) exclusive focus on 24-hour recovery without long-term follow-up; and (3) exclusion of high-risk populations ($\text{BMI} > 30 \text{ kg/m}^2$), who exhibit heightened susceptibility to opioid-related complications and may theoretically derive greatest benefit from oliceridine.

Acknowledgements

We are grateful to all the patients and families who participated in this study. Thank you also to all the anesthesiologists and surgeons who contributed to this study

Confidentiality {27}

All investigators adhere strictly to confidentiality protocols and ethical standards throughout the trial. Personally identifiable data will be maintained with maximized confidentiality. Confidential information undergoes secure processing/storage protocols, with exclusively anonymized datasets shared for analysis.

Data Availability

De-identified participant data generated in this study will be made accessible upon reasonable request to the corresponding author following article publication.

Conflicts of Interest

None declared.

Multimedia Appendix 1

SPIRIT checklist.

Dissemination plans {31a}

Study findings will be submitted for publication in peer-reviewed anesthesiology journals.

Plans to give access to the full protocol, participant level-data and statistical code {31c}

Access to trial data and protocols is exclusively restricted to the trial leader. No personnel may access participant data without documented prior approval from the principal investigator.

Authors' contributions

Jia Han and Yu-Hang Shou conceptualized and designed the trial and drafted the initial protocol; Yu-Hang Shou prepared the preliminary manuscript; Jia Han and Xian-Jie Zhang finalized the manuscript; Jian-Sheng Luo and Wen-Hu Zhai were responsible for participant recruitment and allocation. All authors have read and approved the final manuscript.

References

1. Vitale SG, Giannini A, Carugno J, van Herendael B, Riemma G, Pacheco LA, Drizi A, Mereu L, Bettocchi S, Angioni S *et al*: **Hysteroscopy: where did we start, and where are we now? The compelling story of what many considered the "Cinderella" of gynecological endoscopy.** *Arch Gynecol Obstet* 2024, **310**(4):1877-1888.
2. Buzzaccarini G, Alonso Pacheco L, Vitagliano A, Haimovich S, Chiantera V, Török P, Vitale SG, Laganà AS, Carugno J: **Pain Management during Office Hysteroscopy: An Evidence-Based Approach.** *Medicina (Kaunas)* 2022, **58**(8).
3. Huang L, Yu Q, Zhu Z, Huang P, Ding X, Ma X, Chen Y, Su D: **The Current Situation of Anaesthesia for Hysteroscopy in Mainland China: A National Survey.** *J Pers Med* 2023, **13**(10).
4. Biela MM, Doniec J, Szafarowska M, Sobocinski K, Kwiatkowski A, Kamiński P: **Is every patient eligible to have an office hysteroscopy? A retrospective analysis of 1301 procedures.** *Wideochir Inne Tech Maloinwazyjne* 2020, **15**(2):337-345.
5. Anesthesiology CSocAV: **Expert consensus on anesthesia management in hysteroscopic diagnosis and treatment.** *Journal of Clinical Anesthesiology* 2020, **36**(11):1121-1125.
6. Adams TJ, Aljohani DM, Forget P: **Perioperative opioids: a narrative review contextualising new avenues to improve prescribing.** *Br J Anaesth* 2023, **130**(6):709-718.
7. Liu Y, Zhu Y, Fu H: **Tolerability of different doses of oliceridine versus traditional opioids in acute pain management: a systematic review and meta-analysis.** *Sci Rep* 2025, **15**(1):11470.

8. Viscusi ER: **A critical review of oliceridine injection as an IV opioid analgesic for the management of severe acute pain.** *Expert Rev Neurother* 2022, **22**(6):419-426.
9. Wessels E, Perrie H, Scribante J, Jooma Z: **Quality of recovery in the perioperative setting: A narrative review.** *J Clin Anesth* 2022, **78**:110685.
10. Markos Z, Amsalu H, Mekuanint A, Yirga S, Simegn AE, Kassegn A: **Assessment of intermediate phase post anesthesia quality of recovery and its affecting factors.** *BMC Anesthesiol* 2024, **24**(1):342.
11. Kleif J, Waage J, Christensen KB, Gögenur I: **Systematic review of the QoR-15 score, a patient- reported outcome measure measuring quality of recovery after surgery and anaesthesia.** *Br J Anaesth* 2018, **120**(1):28-36.
12. Stark PA, Myles PS, Burke JA: **Development and psychometric evaluation of a postoperative quality of recovery score: the QoR-15.** *Anesthesiology* 2013, **118**(6):1332-1340.
13. listed Na: **The Use of Hysteroscopy for the Diagnosis and Treatment of Intrauterine Pathology: ACOG Committee Opinion Summary, Number 800.** *Obstet Gynecol* 2020, **135**(3):754-756.
14. listed Na: **ACOG Technology Assessment No. 13 Summary: Hysteroscopy.** *Obstet Gynecol* 2018, **131**(5):1.
15. Yen CF, Chou HH, Wu HM, Lee CL, Chang TC: **Effectiveness and appropriateness in the application of office hysteroscopy.** *J Formos Med Assoc* 2019, **118**(11):1480-1487.
16. De Silva PM, Smith PP, Cooper NAM, Clark TJ: **Outpatient Hysteroscopy: (Green-top Guideline no. 59).** *Bjog* 2024, **131**(13):e86-e110.
17. ji M, Zhang Y-Z, Wu Y, Deng X-F: **Clinical trial of cis-atracurium in the treatment of patients with hysteroscopic surgery.** *The Chinese Journal of Clinical Pharmacology* 2024, **40**(18):2640-2644.
18. Mauermann E, Clamer D, Ruppen W, Bandschapp O: **Association between intra-operative fentanyl dosing and postoperative nausea/vomiting and pain: A prospective cohort study.** *Eur J Anaesthesiol* 2019, **36**(11):871-880.
19. Hoshijima H, Takeuchi R, Kuratani N, Nishizawa S, Denawa Y, Shiga T, Nagasaka H: **Incidence of postoperative shivering comparing remifentanyl with other opioids: a meta-analysis.** *J Clin Anesth* 2016, **32**:300-312.
20. de Boer HD, Dettriche O, Forget P: **Opioid-related side effects: Postoperative ileus, urinary retention, nausea and vomiting, and shivering. A review of the literature.** *Best Pract Res Clin Anaesthesiol* 2017, **31**(4):499-504.
21. Forget P: **Opioid-free anaesthesia. Why and how? A contextual analysis.** *Anaesth Crit Care Pain Med* 2019, **38**(2):169-172.
22. Bergese SD, Brzezinski M, Hammer GB, Beard TL, Pan PH, Mace SE, Berkowitz RD, Cochrane K, Wase L, Minkowitz HS *et al*: **ATHENA: A Phase 3, Open-Label Study Of The Safety And Effectiveness Of Oliceridine (TRV130), A G-Protein Selective Agonist At The μ -Opioid Receptor, In Patients With Moderate To Severe Acute Pain Requiring Parenteral Opioid Therapy.** *J Pain Res* 2019, **12**:3113-3126.
23. Gan TJ, Wase L: **Oliceridine, a G protein-selective ligand at the μ -opioid receptor, for the management of moderate to severe acute pain.** *Drugs Today (Barc)* 2020, **56**(4):269-286.
24. Soergel DG, Subach RA, Burnham N, Lark MW, James IE, Sadler BM, Skobieranda F, Violin JD, Webster LR: **Biased agonism of the μ -opioid receptor by TRV130 increases analgesia and reduces on-target adverse effects versus morphine: A randomized, double-blind, placebo-controlled, crossover study in healthy volunteers.** *Pain* 2014, **155**(9):1829-1835.
25. Viscusi ER, Webster L, Kuss M, Daniels S, Bolognese JA, Zuckerman S, Soergel DG, Subach RA, Cook E, Skobieranda F: **A randomized, phase 2 study investigating TRV130, a biased ligand of the μ -opioid receptor, for the intravenous treatment of acute pain.**

- Pain* 2016, **157**(1):264-272.
26. Singla N, Minkowitz HS, Soergel DG, Burt DA, Subach RA, Salamea MY, Fossler MJ, Skobieranda F: **A randomized, Phase IIb study investigating oliceridine (TRV130), a novel μ -receptor G-protein pathway selective (μ -GPS) modulator, for the management of moderate to severe acute pain following abdominoplasty.** *J Pain Res* 2017, **10**:2413-2424.
 27. Singla NK, Skobieranda F, Soergel DG, Salamea M, Burt DA, Demitrack MA, Viscusi ER: **APOLLO-2: A Randomized, Placebo and Active-Controlled Phase III Study Investigating Oliceridine (TRV130), a G Protein-Biased Ligand at the μ -Opioid Receptor, for Management of Moderate to Severe Acute Pain Following Abdominoplasty.** *Pain Pract* 2019, **19**(7):715-731.
 28. Bu XS, Zhang J, Zuo YX: **Validation of the Chinese Version of the Quality of Recovery-15 Score and Its Comparison with the Post-Operative Quality Recovery Scale.** *Patient* 2016, **9**(3):251-259.

Fig. 1. The flowchart for this study.

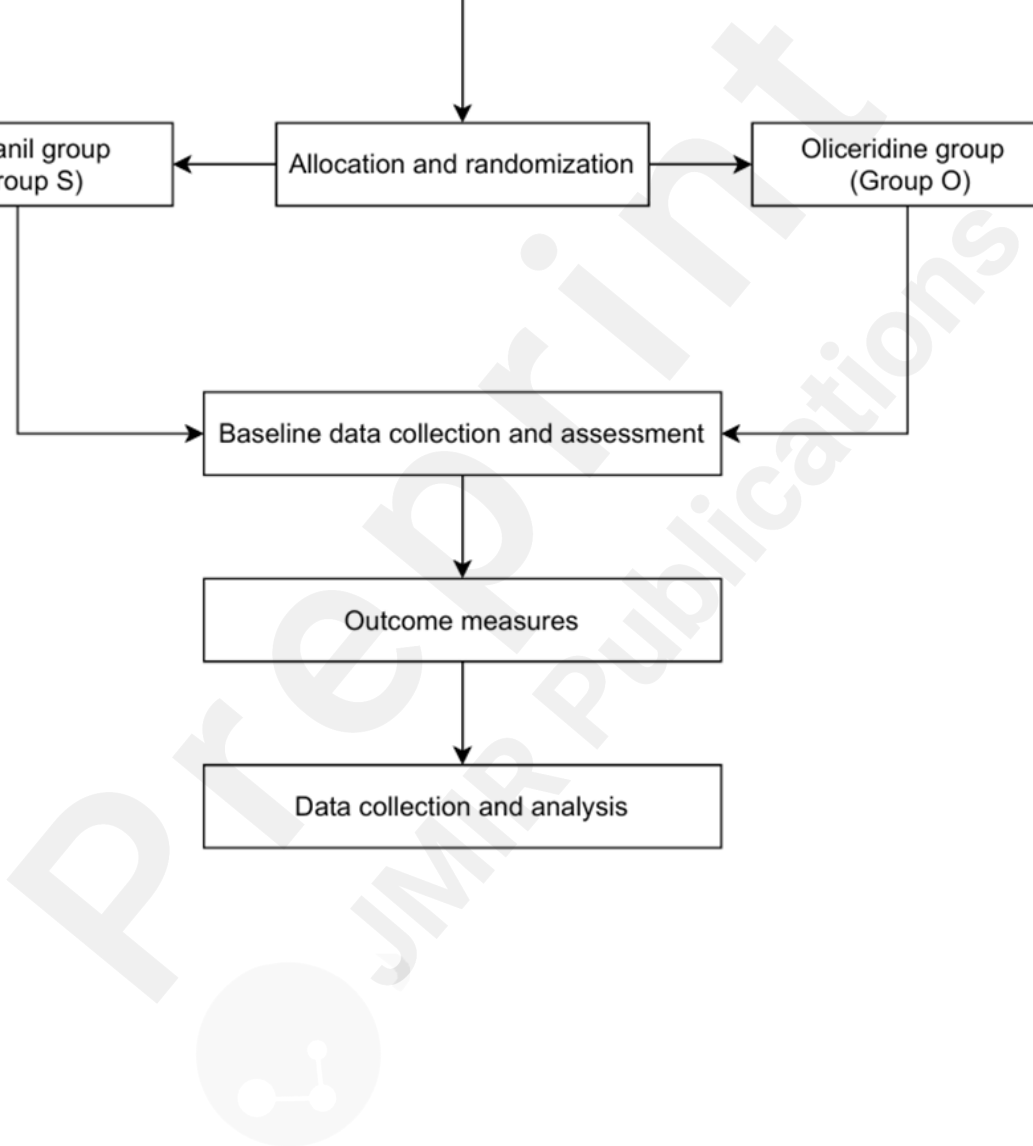


Fig. 2. The study schedule of the enrollment, interventions, and assessments.

	STUDY PERIOD			
	Enrolment	Allocation	Surgery	Follow-up phase
TIMEPOINT**	<i>Day – 1</i>	<i>Before surgery</i>	<i>During anesthesia</i>	<i>Within 24hrs after surgery</i>
ENROLMENT:				
Eligibility screen	X			
Informed consent	X			
Allocation		X		
INTERVENTIONS:				
<i>[Intervention S]</i>			X	
<i>[Intervention O]</i>			X	
ASSESSMENTS:				
<i>[Baseline data]</i>	X			
<i>[Primary outcome]</i>				X
<i>[Secondary outcome]</i>			X	X

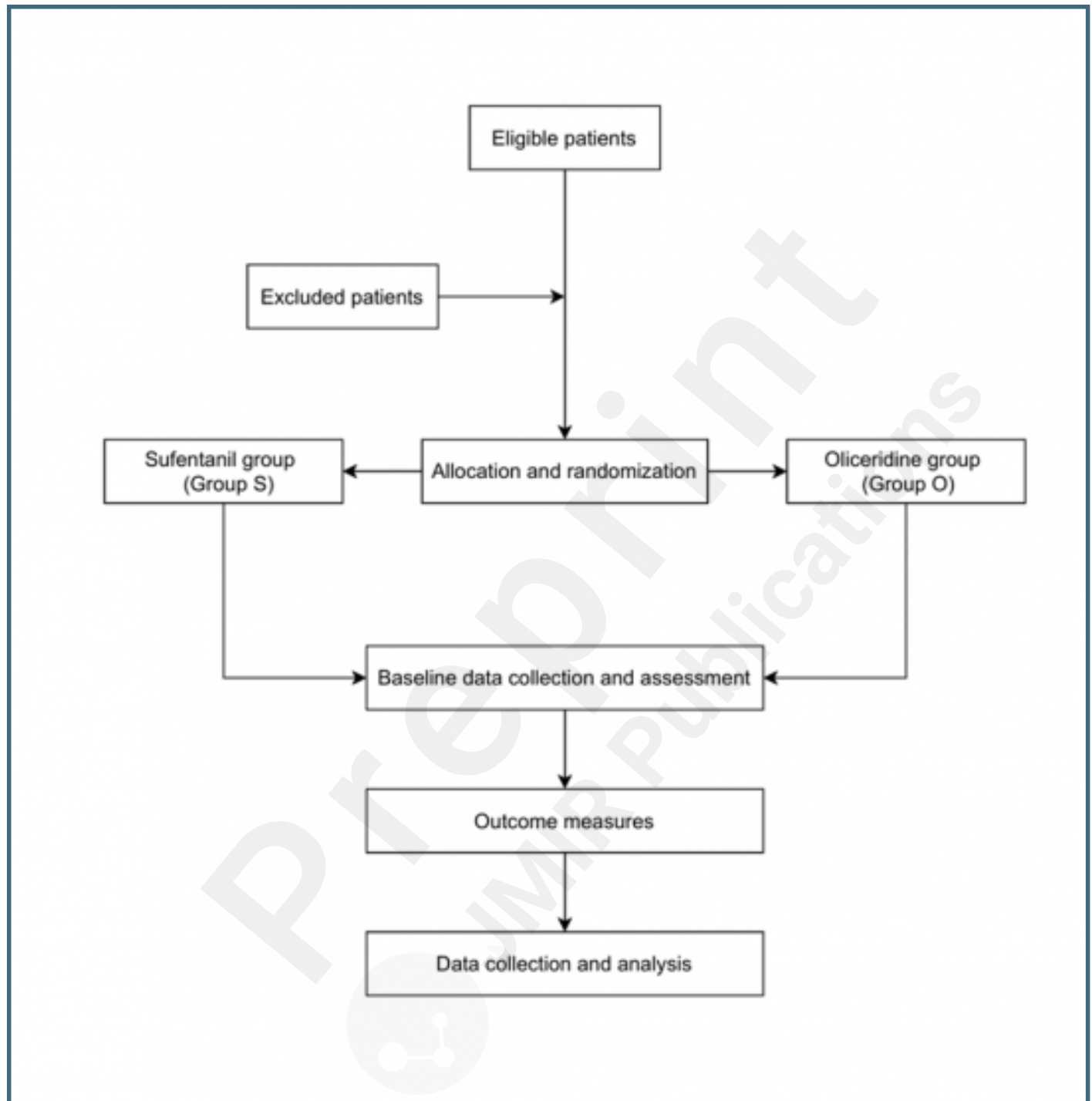
Supplementary Files

SPIRIT checklist.

URL: <http://asset.jmir.pub/assets/9c7d8969db1f29f21991fe4551c2f1fc.docx>

Figures

The flowchart for this study.



The study schedule of the enrollment, interventions, and assessments.

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Allocation		X		
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<i>[Intervention S]</i>			X	
<i>[Intervention O]</i>			X	
ASSESSMENTS:				
<i>[Baseline data]</i>	X			
<i>[Primary outcome]</i>				X
<i>[Secondary outcome]</i>			X	X