The Second Xiangya Hospital Central South University Clinical Research Informed Consent Form

Dear Participant/Volunteer:

We invite you to participate in a medical study titled "Series Study on the Application of G Protein-Biased Receptor Agonist Oliceridine in Gynecological Surgery Based on ERAS Principles (2): Effects of Oliceridine Versus Sufentanil on Postoperative Nausea and Vomiting After Gynecological Laparoscopic Surgery" which is being conducted by the Department of Anesthesiology, the Second Xiangya Hospital of Central South University. Your participation in this study is entirely voluntary. To assist you in understanding this study, this informed consent form will provide you with detailed information regarding the purpose of the study and its procedures, as well as a specific explanation of the potential risks involved in participation and any potential benefits. If you are interested, please read the following information carefully. The study physician and research staff will explain any questions you may have in detail. If all your questions about this study have been satisfactorily addressed and you are considering participation, you may sign this informed consent form.

I. Why is this study being conducted?

Postoperative nausea and vomiting (PONV) is a common complication following surgery and constitutes a major obstacle to rapid postoperative recovery. According to reports, the incidence of PONV among all postoperative patients is 30%, and can reach as high as 80% in high-risk patients. Risk factors include female sex, age under 50 years, non-smoking status, a history of PONV or motion sickness, and opioid use. Therefore, gynecological surgery involves multiple risk factors for the development of PONV. PONV not only results in an unpleasant hospitalization experience for patients, but more importantly, it can lead to fluid loss, water-electrolyte imbalance, and weakness—complications that are considered more serious than pain following surgery. In cases where severe nausea and vomiting occur postoperatively, complications such as aspiration, esophageal tear, subcutaneous emphysema, pneumothorax, and incisional hernia may arise. Furthermore, PONV prolongs hospital stays, increases medical costs, and decreases patient satisfaction with their hospitalization. Therefore, exploring effective methods to reduce PONV is of significant clinical relevance. Opioids remain commonly used medications for moderate to severe acute pain; however, conventional opioids increase the risk of PONV in a dose-dependent manner. In recent years, the novel G protein-biased receptor agonist oliceridine has been developed. It is an opioid that selectively activates the G protein signaling pathway rather than the β-arrestin pathway. The oliceridine injection solution package insert clearly states that it is indicated for the treatment of severe acute pain in adult patients requiring intravenous opioid therapy. During gynecological surgery in adults, opioids are needed for pain control; therefore, the use of oliceridine injection solution for the management of acute pain in gynecological surgery is consistent with the drug's approved indications. Additionally, oliceridine provides safe and effective analgesia while

offering significant advantages in gastrointestinal tolerance, which may support its rational use in gynecological surgery and improve perioperative comfort for gynecological patients. Therefore, we hypothesize that oliceridine may reduce the incidence of PONV during analgesia for gynecological surgery. This study is designed to investigate whether the use of oliceridine in common gynecological laparoscopic surgeries can decrease the incidence of PONV and facilitate rapid patient recovery.

II. Study Procedures

(1) Screening and Grouping

Inclusion criteria: Elective gynecological laparoscopic surgery; age 18–65 years; American Society of Anesthesiologists (ASA) classification I–III; BMI 18–30 kg/m².

Exclusion criteria: Severe dysfunction of major organs such as the heart, lungs, or brain; history of allergy to opioids, propofol, soybeans, or eggs; recent use of sedatives, analgesics, or monoamine oxidase inhibitors; history of alcohol abuse; obstructive sleep apnea syndrome; difficult airway; psychiatric or neurological disorders, or communication disorders; women who are breastfeeding or pregnant.

Withdrawal criteria: (1) The participant requests or voluntarily chooses to withdraw; (2) Change in surgical approach requiring combined gastrointestinal surgery; (3) Allergic reaction to the investigational drug or occurrence of life-threatening complications; (4) Reoperation within 48 hours due to postoperative bleeding or other causes.

This study is a randomized controlled trial comprising a control group (sufentanil group) and an oliceridine group. Patients who meet the inclusion criteria will sign the informed consent form and be randomly assigned to either the experimental group or the control group, with 48 participants in each group. The probability of being assigned to the experimental group is 50%.

(2) Study Protocol

After enrollment in the study, patients will receive sequential intravenous injections of midazolam 0.05–0.10 mg/kg and sufentanil 0.3 μg/kg (sufentanil group) or oliceridine (0.06 mg/kg, calculated based on the oliceridine injection solution instructions, where 1 mg of oliceridine is approximately equivalent in potency to 5 mg of morphine), Propofol 1.5–2.0 mg/kg, and cisatracurium 0.2–0.3 mg/kg. After intubation, both groups of patients received volume-controlled mechanical ventilation with a tidal volume of 6–8 ml/kg, a respiratory rate of 8–12 breaths per minute, and an inspiratory-to-expiratory ratio of 1:2. Ventilation parameters were adjusted to maintain PCO2 at 35–40 mmHg (1 mmHg = 0.133 kPa). Prior to skin incision, an additional dose of sufentanil 0.1–0.2 μg/kg (sufentanil group) or oliceridine 0.02–0.04 mg/kg (oliceridine group) was administered. Intraoperatively, total intravenous anesthesia was maintained with continuous infusion of Propofol at 4–10 mg/kg/h, continuous intravenous infusion of Remifentanil at 0.1–0.2 μg/kg/min, and intermittent intravenous injection of Cisatracurium Besylate 4 mg. Approximately 30 minutes before the end of surgery, sufentanil 0.1 μg/kg (sufentanil group) or oliceridine 0.02 mg/kg (oliceridine group) was administered. If the patient experiences PONV of grade 2 or higher, a combination of ondansetron 4 mg and dexamethasone 5 mg will be administered

intravenously. If symptoms persist after one hour, haloperidol 1 mg will be added for treatment. Postoperative analgesia regimen: In the sufentanil group, sufentanil 2 μg/kg; in the oliceridine group, oliceridine 0.4 mg/kg; along with ondansetron 8 mg and dexamethasone 10 mg, diluted with normal saline to a total volume of 100 ml. The initial loading dose is 2 ml, with no background infusion; each bolus is 2 ml, with a lockout interval of 10 minutes, and a maximum of 10 ml per hour. All enrolled patients will be connected to an electronic analgesia pump immediately after surgery. Prior to surgery, the usage of the electronic analgesia pump will be explained to both patients and their families. If postoperative pain cannot be alleviated by the analgesia pump, the anesthesiologist will administer a rescue dose of either sufentanil 5 μg or oliceridine 0.2 mg as needed. If the rescue intervention is ineffective, the anesthesiologist will determine alternative remedial measures and record the medications and dosages administered.

The indicators to be collected include:

General information: including age, height, weight, BMI, ASA classification, smoking history, previous history of PONV, history of motion sickness, surgical history, history of hypertension, and history of diabetes.

Intraoperative indicators include: surgical approach, surgical site, blood loss, duration of surgery, duration of anesthesia, dosage of anesthetic agents, infusion volume, and other relevant parameters.

Primary outcome measure: incidence of PONV within 48 hours after surgery. PONV will be assessed in the ward within 48 hours after surgery by a blinded evaluator. Participants are required to complete a simplified PONV impact scale regarding whether they have experienced any PONV events in the past 48 hours and to provide ratings. (The scale consists of two questions: Q1. Have you experienced vomiting or symptoms of vomiting? If so, how many times in total? Under what circumstances did it occur? Was medication used for treatment? Q2. Have you experienced nausea? If so, did the nausea affect your daily activities? Was medication used for treatment?) Based on the frequency, number, and triggers of nausea and vomiting, PONV is classified into four grades: Complete response is defined as no vomiting or nausea not requiring rescue therapy; mild PONV is defined as mild nausea induced by drinking or movement, or a single episode of vomiting; moderate PONV is defined as two episodes of vomiting or significant nausea requiring rescue therapy; severe PONV is defined as more than two episodes of vomiting or the need for more than one dose of rescue therapy.

Secondary outcome measures:

Incidence of PONV across four time intervals (T1: PACU stay; T2: from PACU discharge to 12 hours postoperatively; T3: 12 to 24 hours postoperatively; T4: 24 to 48 hours postoperatively): Incidence of postoperative vomiting (POV) and POV scores during each of the four time intervals (T1－T4) within 48 hours after surgery. Usage of rescue antiemetic medications.

Postoperative analgesia: Resting visual analogue scale (VAS) pain scores during the four time intervals (T1－T4) within 48 hours after surgery, measured using a 10 cm sliding scale with numbers 0－10 on the reverse side, where '0' on the left indicates no pain and '10' on the right indicates

unbearable severe pain. Record the number of PCA presses, total analgesic consumption, and the use of rescue analgesics within 48 hours after surgery.

Ramsay sedation score at 2 hours postoperatively: a score of 1 indicates agitation, 3 or 4 indicates drowsiness, and 5 or 6 indicates excessive sedation.

Sleep quality score on the night after surgery: The patient's sleep quality will be assessed using a numerical rating scale. An 11-point Likert scale ranging from 0 to 10 will be used, where 0 represents complete insomnia and extremely poor sleep quality, and 10 represents excellent sleep quality. A score of 0–3 indicates severe insomnia, 4–6 indicates moderate insomnia, and 7–10 indicates good sleep quality. 5) Aldrete Score: The modified Aldrete score will be used as the criterion for assessing recovery of consciousness, with a score of 9 or above indicating adequate emergence from anesthesia.

QOR-15 Score: 0 points indicate extremely poor quality of recovery, while 150 points indicate excellent quality of recovery. Assessments will be conducted preoperatively, on the first postoperative day, and on the third postoperative day.

Duration of stay in the recovery room, time to first postoperative bowel movement, time to resumption of drinking, time to first postoperative food intake, time to first ambulation after surgery, and any other adverse events.

Medications or Procedures Prohibited in the Study

The recent use of sedatives, analgesics, monoamine oxidase inhibitors, and similar medications is prohibited in this study.

III. Related Benefits

Participant Benefits:

Participants will be exempt from perioperative anesthesiology pain assessment fees (clinical scale), valued at 36 yuan.

Potential benefits for participants in this study include: 1) improved postoperative analgesia, reduced pain, and enhanced comfort during recovery; 2) reduced incidence of postoperative nausea and vomiting, leading to improved postoperative quality of life; 3) provision of a novel treatment option that may offer better management of postoperative pain and nausea and vomiting, especially for patients who are resistant to or experience adverse effects from traditional opioids; and 4) reduced economic and physical burdens associated with severe vomiting.

The oliceridine injection solution package insert clearly states that it is indicated for the treatment of severe acute pain in adult patients requiring intravenous opioid therapy. During gynecological surgery in adults, opioids are needed for pain control; therefore, the use of oliceridine injection solution for the management of acute pain in gynecological surgery is consistent with the drug's approved indications. Additionally, oliceridine provides safe and effective analgesia while offering significant advantages in gastrointestinal tolerance, which may support its rational use in gynecological surgery and improve perioperative comfort for gynecological patients.

This study will be conducted within the approved indications for the drug, which has been procured through standard hospital bidding procedures.

Therefore, no additional costs will be incurred by the participant. All examinations in this study are routine clinical assessments, and there will be no additional tests or increased frequency of examinations.

IV. Potential Risks and Discomforts

This study will be conducted according to standard clinical pathways. The study drugs are opioids and may cause opioid-related side effects and adverse reactions, such as respiratory depression, nausea and vomiting, as well as other opioid-related effects. If you experience any discomfort, new changes in your condition, or any unexpected events—regardless of whether they are related to the medication—you should promptly inform the study physician, who will assess the situation and provide appropriate medical management.

5. Procedures for Handling Issues During the Study

If you experience any adverse events during the study that are determined by the investigator to be caused by the study medication or the diagnostic procedures required by the study protocol, and these events result in harm to you, you may receive appropriate treatment at the research hospital where you are participating. If you experience any discomfort during the study, please promptly contact your physician, Dr. Xia Shuangyin, at 18670781546.

6. Information Confidentiality

If you decide to participate in this study, both your participation and your personal information within the study will be kept confidential. Relevant laws in our country provide safeguards for the security of privacy, data, and authorized access. When collecting and processing information related to you for this study, we will strictly comply with legal requirements to keep your information confidential. Unless required by applicable laws, your name, identification number, address, telephone number, or any information that can directly identify you in the study records will not be disclosed. The principal investigator and other research staff will use your medical information for the study. This information may include your name, address, telephone number, medical history, and information obtained during your study visits. To ensure the study is conducted in compliance with regulations, the investigator, sponsor, regulatory authorities, or members of the ethics committee may, when necessary and in accordance with regulations, review your personal information at the study site.

VII. Refusal to Participate or Withdrawal from the Study

Participation in this study is entirely voluntary. You may refuse to participate or withdraw from the study at any stage and in any manner, without discrimination or retaliation. Your medical treatment and rights will not be affected. However, you are required to return all unused study drugs and devices.

If you experience a severe adverse reaction, or if your study physician determines that continued participation is not in your best interest, he or she may decide to withdraw you from the study. If any of the above situations arise,

we will notify you promptly, and your study physician will discuss with you the alternative options available. If the physician believes that an abrupt interruption of the trial may affect your health, you may be required to come to the hospital for an examination before discontinuing the trial. After a participant withdraws, no new data related to them will be collected.

VIII. Relevant Consultation

If you have any questions related to this study, please contact Dr. Xia Shuangyin at 18670781546. If you have any concerns regarding your personal rights, or if you wish to express any dissatisfaction experienced during your participation in this study,

please contact the Office of the Clinical Research Ethics Committee at the Second Xiangya Hospital of Central South University. Telephone: 0731-85292476

Participant Statement and Signature Confirmation:

I have carefully read this informed consent form and have had the opportunity to ask questions. The research staff has provided thorough explanations and answered my questions. I understand that participation in this study is entirely voluntary, and that I may withdraw at any time without providing a reason. My medical care and legal rights will not be affected. I permit the researchers, health administrative authorities, institutional staff, and ethics committee members to review my medical records. I am aware that the researchers will take all reasonable measures to protect my privacy. I agree to participate in this study and will receive a signed copy of the complete informed consent form.

Participant Name (printed):
Signature (handwritten): Date:
Contact Number:
Participant’s Legal Representative Name (printed):
Signature (handwritten): Date:
Contact Number:

Researcher Statement and Signature Confirmation:

I or my research staff have fully explained to the participant the purpose of this clinical trial, the study procedures, and the potential risks and benefits of participation, and have answered all questions raised by the participant.

Designated project contact: Phone number:___ _____

Investigator’s name (printed):
Signature (handwritten): Date:
Phone number: