Informed Consent Notification Page

Dear patients,

We sincerely invite you to participate in a trial named *Comparison of Hydromorphone-Based Intravenous Patient-controlled Analgesia with and without Low Basal Infusion on Postoperative Hypoxemia After Gastrointestinal surgery*. Before deciding whether to participate in this study, please read the following contents as carefully as possible, which can help you: 1. To understand the study’s background knowledge, purpose, and interests; 2. To know the procedure and duration of the research; 3. Identify the benefits, discomfort, and risks that may be brought to you by participating in the study. If you wish, you can also discuss this with your relatives or friends or ask your managing physician for an explanation to help you decide whether to participate in this clinical study. If you have any questions, please refer them to the anaesthesiologist in charge of the research.

**I. Background and purpose**

Patient-controlled intravenous analgesia (PCIA), commonly known as intravenous analgesia pump in Chinese, is a kind of analgesia technique that patients wear with a sophisticated microprocessor-controlled infusion pump push a demand button of pumps according to the subjective pain feeling and injects the drug into the body, to achieve the purpose of relieving pain on-demand. PCIA (with or without a continuous background infusion) is common in gastrointestinal surgery due to its advantages of low doses, stable blood drug concentration, and adequate patient dominance. Opioids remain the mainstream drugs used for PCIA, but their potential side effects include nausea and vomiting, itching, and even respiratory depression. Hydromorphone is a semisynthetic potent opioid analgesic widely used in acute severe pain and PCIA abroad. It has shown a nice analgesic effect in patients with PCIA since approved and marketed in China in 2013. However, there is no clear suggestion for a better infusion mode of hydromorphone in gastrointestinal surgery PCIA due to a few research on postoperative hypoxemia related to hydromorphone PCIA with or without a continuous background infusion. Therefore, we plan to use wireless wearables to monitor the continuous vital signs of patients with PCIA to explore whether low-infusion hydromorphone PCIA is non-inferior compared with those of no basal infusion on postoperative hypoxemia.

**II. Condition for participating in the trial**

In this study, 160 eligible patients undergoing gastrointestinal surgery are expected to participate voluntarily. Everyone is allowed to withdraw from the study at any time without prejudice.

**The inclusion criteria** are as follows:
1. Patients scheduled for elective gastrointestinal tumor resection under general anaesthesia who will receive postoperative PCIA
2. Age > 18 years
3. Body mass index (BMI) 18.5–30 kg/m²
4. American Society of Anesthesiologists grade I–III
5. Voluntary participation and provision of written informed consent

**The exclusion criteria** are as follows:
1. SpO₂ < 90% or chronic severe respiratory disease (chronic obstructive pulmonary disease,
obstructive sleep apnea syndrome)
2. History of chronic pain, analgesic or sedative abuse, or known opioid allergy
3. Kidney disease [serum creatinine concentration > 140 (males) or 130 (females) µmol/L and oliguria/anuria] or renal replacement therapy (e.g., dialysis)
4. Hepatic disease (liver enzyme concentrations twice the normal values)
5. Pregnancy or breastfeeding status
6. Operation time > 5 h
7. Plan for postoperative transfer to the intensive care unit
8. Participation in another clinical trial in the previous three months

III. Study design and procedure
The sponsor of this trial is the Department of Anesthesia and Perioperative Medicine, Fourth Military Medical University Xijing Hospital. The Xijing Hospital Ethics Committee, which conforms to Chinese legislation and the Declaration of Helsinki, approved this study on November 22, 2021 (No. KY20212163-F-1). All the researchers are clinicians with the qualifications of medical practitioners with rescue and other treatment skills, have received clinical trial research training, and obtained GCP certificates.

**Study Design:** This study was a single-centre, randomised, double-blind, parallel-controlled non-inferiority clinical trial.

**Research Procedure:** If you meet the selection criteria and are willing to participate in this study, you will be randomly divided into the no basal or low basal infusion PCIA group. The PCIA drug for both groups will be the same, while the infusion mode will differ. The no basal group provides patient demand dose, while the low basal group will include additional administration of continuous infusion with a low dose. We will show you how to use the analgesic pump, which is easy to operate. No matter which group you are assigned to, you can press the demand button when you feel pain. We will record your necessary data related to the study through the electronic medical record system, interviews, and follow-up. Required information including age, sex, medical history, general routine medical examination (such as blood pressure, heart rate, etc.), laboratory examination (such as haemoglobin, blood gas, etc.), medicine use (such as drug type, dose, etc.), and follow-up to 2 days after the operation. We will collect data on pain, nausea and vomiting, intestinal function, and so on during the postoperative visit. In addition, we will use the wireless wearable device to monitor and record your vital signs in the ward after the operation.

Your treatment group allocation will not affect the doctor’s routine treatment for you. No special examination and treatment items are designed in this study, and the above routine treatment and medical examination items are necessary routine clinical items for surgical patients in the perioperative period.

IV. Benefits of participating in this study
The clinical results obtained from your and other subjects’ participation in this study may contribute to optimising postoperative analgesia for patients with gastrointestinal surgery similar to yours.

V. Potential risks of participating in this study
The hydromorphone used in this study is a common analgesic after gastrointestinal surgery. The possible risk is the risk of routine postoperative analgesias, such as excessive sedation and mild
respiratory depression. Doctors will try their best to prevent and treat the damage that this study may cause. If damage related to the research occurs in the clinical research, compensation will be provided following the “Drug Clinical trial quality Management Standard” of our country. This study has prepared reasonable preservation measures for you, protecting your legitimate rights and interests as much as possible.

VI. Expenses related to participating in this trial
Whether you participate in this study or not, the appropriate diagnosis and treatment measures will be carried out generally following a medical practice. The medicines used in the study are commonly used in the clinic, there is no additional cost, and the patients bear the treatment cost.

VII. Patient confidentiality
After completing this study, we will collate and analyse the information and data collected. The final results and conclusion will be compiled and published. Your name will be replaced by pinyin abbreviations in all the medical records of the study. Your medical records and materials will be kept in the hospital, and your medical records can be accessed with the approval of researchers, research authorities, and ethics committees. Any public report on the results of this study will not disclose your identity.

VIII. Your rights
Your or your relatives’ participation in the study is entirely voluntary. You or your relatives can withdraw from the study at any time without any reason, which will never affect your or your relatives’ and medical staff’s relationship and any future medical treatment and rights; all personal data and observation records of you or your loved ones are confidential and are for the use of this study only. During the study, you can learn about the relevant information at any time, such as when there are problems in the research or you need to consult the relevant questions, you can ask your managing physician. If you still have any questions or encounter an emergency, contact the project leader: Doctor Nie Huang, deputy chief physician, at tel 029-84775343.

IX. Contact information of the Ethics Committee
The trial protocol has been approved and implemented by the hospital ethics committee. If there is any violation of the research protocol during the trial, you can complain directly to the hospital ethics committee. Tel: 029-84771794, email: xjyllwyh@163.com.
Subject Informed Consent Signature Page

I have read the above informed consent form in detail and understood the purpose of the study and the possible benefits and risks of participating in the study. The researchers have clearly explained the above medical terms. I had the opportunity to ask questions, and all of them got easy-to-understand answers. I can choose not to participate in this study or withdraw after notifying the doctor in charge at any time, and any of my medical treatment, rights, and interests will not be affected. If I need other treatment, if I do not comply with the research plan, if there is a study-related injury, or if there is any other reason, the responsible doctor can terminate my participation in this study.

I have read the above informed consent form and obtained a copy, and my managing physician has given me a detailed explanation. I volunteered to participate in this clinical trial. I agree that the concerned authorities should check the data collected by the experimental study against my original medical records.

Subject name in regular script: ___________________
Signature of subject: ___________________
Subject phone number: ___________________ Date: ___yy / ___mm / ___dd

(note: when the subject has no capacity for civil conduct, the guardian’s signature is required; when the subject is limited to the capacity for civil conduct, the subject and his guardian need to sign)

Guardian name in regular script: _________________
Relationship with subject: _________________
Signature of guardian: _________________
Guardian telephone number: _________________ Date: ___yy / ___mm / ___dd

(If the subject or his guardian is unable to read, a fair witness is required to sign, and the fair witness reads the informed consent form and other written materials and witnesses informed consent.)

Signature of fair witness (if applicable): ______________ Date: ___yy / ___mm / ___dd

I confirm that I have explained to the patient in detail the relevant contents of this clinical trial, including the possible benefits and risks, and answered all the questions raised by the patient.

Researcher name in regular script: _______________
Signature of researcher: _______________
Researcher phone number: _______________ Date: ___yy / ___mm / ___dd