INFORMED CONSENT FORM

Study Title	Liposomal Bupivacaine versus Ropivacaine Hydrochloride for Post-Operative Analgesia Management after Haemorrhoidectomy
Principal Investigator	Bai Yonggang
Department	Department of Anesthesiology
Informed Consent Form Version No.	1.0
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Dear Sir/Madam,

We are going to conduct a prospective, randomized controlled clinical trial entitled “Liposomal Bupivacaine versus Ropivacaine Hydrochloride for Post-Operative Analgesia Management after Haemorrhoidectomy”. You are invited to take part because you meet the eligibility criteria for this study. The principal clinical investigator of this study is Dr. Sun Bo from the Department of Anesthesiology, Tongliao People’s Hospital. Approximately 150 subjects will voluntarily participate in this trial.

This informed consent document describes the study purpose, procedures, potential benefits, risks, inconveniences and your rights. Please read it carefully before you decide whether to join the study. When the researcher explains this document to you, you may ask questions at any time and request clarification for anything you do not understand. You may also discuss this study with your family members, friends or attending physician before making your decision.

If you are currently participating in another clinical research study or taking certain medications, please inform the research staff or your study physician.

Important statement: Your decision to decline participation will not affect your routine medical care or your participation in other research or educational activities at Tongliao People’s Hospital. Biological samples and medical record information collected for this research will be securely stored. Your right to decide on secondary use of samples and your privacy will be fully protected.

Please read the full Informed Consent Form below.

Background and Study Purpose

Haemorrhoidectomy is a common anorectal surgical procedure. Severe and prolonged postoperative pain may impair patient rehabilitation and quality of life. Conventional analgesia mainly relies on opioids, which carry side-effects such as respiratory depression, nausea and vomiting. Traditional local anaesthetics such as ropivacaine hydrochloride have a short duration of action (approximately 8-12 hours) and often fail to cover the full postoperative pain period. Consequently, patients frequently require opioid rescue analgesia, which may lead to nausea, constipation and addiction-related risks. Long-acting analgesia may shorten hospital stay, reduce medical costs and improve patient satisfaction by facilitating early functional recovery. Therefore, investigating long-acting, safe local anaesthetics that reduce opioid dependence is clinically meaningful.

Liposomal bupivacaine injection utilises DepoFoam technology to sustain bupivacaine release for up to 72 hours. It received FDA approval for wound-infiltration analgesia after haemorrhoidectomy in 2011. Liposomal bupivacaine has been approved for marketing in China since 2024; however, clinical data in anorectal surgery remain limited. High-quality direct comparative evidence regarding efficacy, safety and recovery benefits between liposomal bupivacaine and ropivacaine in haemorrhoidectomy is lacking and needs to be established to optimise analgesic strategies.

This study aims to compare postoperative analgesic efficacy and adverse events between liposomal bupivacaine and ropivacaine hydrochloride in patients undergoing haemorrhoidectomy, so as to provide clinical evidence for the application of liposomal bupivacaine in anorectal surgery.

Study Population

Inclusion Criteria

1. Age between 40-60 years old
2. Scheduled for haemorrhoidectomy
3. ASA physical status classification I-III
4. BMI ranging from 18-30 kg/m^2

Exclusion Criteria

1. Pre-existing acute or chronic pain other than surgical pain
2. Advanced malignancy with ascites or widespread metastasis; receiving systemic chemotherapy/radiotherapy; or scheduled for postoperative hyperthermic intra-peritoneal perfusion
3. Pregnancy, lactation or planned pregnancy

4. Known allergy or contraindication to study anaesthetics, adjuvant analgesics, rescue analgesics, anti-emetics or antibiotics

5. Chronic opioid therapy or any analgesic administered within 48 hours prior to surgery

6. Obstructive sleep apnoea syndrome

7. Psychiatric or neurological disorders, gastrointestinal obstruction, chronic obstructive pulmonary disease, cor pulmonale, cardiovascular diseases, etc.

8. Systemic corticosteroids (oral, inhaled or parenteral) administered within 3 months before surgery

Withdrawal Criteria

1. Post-operative insufficient arousal, delirium or behavioural disturbance precluding study assessments

2. Severe postoperative haemodynamic instability or respiratory insufficiency

3. Other conditions judged by investigators to render continued study participation inappropriate

Study Methods

Subjects will be allocated by random-number table. Investigators assign participants to study groups according to randomisation results.

1. Vital-sign monitors will be connected before anaesthesia. Spinal subarachnoid block will be performed using the Tuoren disposable anaesthesia puncture kit (Model AS-SII).

2. Spinal block will be performed by an experienced anaesthesiologist; ultrasound guidance may be used at the operator's discretion. Before dural puncture, 2-3 mL of 2% lidocaine will be injected for local skin infiltration. Puncture site will be L3-4. After free-flow of cerebrospinal fluid is confirmed and no blood is aspirated, 3 mL of 0.5% ropivacaine hydrochloride will be injected intrathecally.

3. At the end of surgery, subjects will receive perianal sphincter-wound infiltration according to random-envelope group assignment. Infiltration will be performed by the same anaesthesiologist using six 5 mL syringes to maintain blinding.

4. Intra-procedural complications such as intravascular injection and paraesthesia will be recorded. All operations will be performed under spinal (non-general) anaesthesia. If painful response is elicited by forceps clamping at the surgical site before surgical incision, inadequate block will be diagnosed. Such patients may receive conversion to general anaesthesia and will be excluded from data analysis.

Outcome Assessments

Primary efficacy endpoint: Analgesic effect at multiple time-points within 48 hours after wound-infiltration administration.

Assessments will be conducted at 1 h, 2 h, 4 h, 6 h, 12 h, 24 h and 48 h post-infiltration. The primary evaluation metric is the Numeric Rating Scale (NRS) pain score within 48 hours.

Secondary observations:

1. Incidence of respiratory depression (defined as respiratory rate ≤8 breaths/min or SpO_2 < 90%), nausea and vomiting within 48 hours after infiltration
2. Haemodynamic parameters (heart rate, blood pressure) within 48 hours after infiltration
3. Ramsay Sedation Scale scores within 48 hours after infiltration
4. Rescue analgesia rate within 48 hours after infiltration
5. Total consumption of parecoxib sodium within 48 hours after infiltration
6. QoR-15 score, patient satisfaction, time to first ambulation, time to first oral intake, time to first flatus and defecation, length of hospital stay, etc.

Alternative Treatment Options

You may choose not to participate in this research, and this will not compromise your standard clinical care. You will not receive discriminatory treatment. Standard postoperative analgesic regimens include opioid-based agents such as hydromorphone. If you decline study enrolment, you may discuss alternative treatment options with your attending physician.

Potential Benefits

Haemorrhoidectomy causes perianal trauma; postoperative perianal pain and tenesmus are common complaints that interfere with rest, defecation and daily activities. Both study medications are approved clinical analgesics. Liposomal bupivacaine provides prolonged sustained analgesia; ropivacaine hydrochloride offers rapid onset and stable pain control. If you take part, you will receive standardised postoperative analgesia that may reduce acute and recovery-phase wound pain, relieve suffering and improve postoperative sleep, oral intake and defecation, enhancing rehabilitation comfort.

Compared with routine clinical practice, study-specified dosage, administration and follow-up are strictly standardised, which may reduce risks of insufficient analgesia or non-standard medication and provide reliable pain control.

During study participation, free specialised postoperative follow-up and physical assessments will be provided by the research team, including pain-score evaluation, perianal wound inspection, vital-sign monitoring and adverse-event screening at postoperative 4 h, 6 h, 12 h, 24 h and 48 h. All assessments are free of charge. Collected data will be used solely for research analysis.

Study clinicians will monitor your recovery, detect abnormal pain, wound oedema or minor complaints early, and provide professional rehabilitation guidance, medication advice and nursing recommendations to support safe and rapid recovery.

Potential Risks

Drug-related risks

1. Local numbness and paraesthesia: Both study drugs are local anaesthetics; postoperative transient perianal numbness and hypo-sensitivity are expected pharmacological effects. Numbness may persist longer with liposomal bupivacaine owing to its prolonged duration; symptoms resolve completely after drug metabolism without permanent nerve injury. Rarely, transient perianal stinging, formication or aggravated tenesmus may occur and usually resolve spontaneously.

2. Local erythema and pruritus: In rare susceptible individuals, mild local allergic reactions (erythema, pruritus, rash at injection site) to drug excipients may occur. Symptoms are usually mild and resolve rapidly with symptomatic management without long-term sequelae.

3. Local haematoma and worsened oedema: The perianal region is highly vascular. Rare micro-vascular injury during infiltration may cause minor haematoma or aggravated perianal oedema. Research staff will take intra- and post-operative precautions. If these events occur, symptomatic measures such as cold compresses and anti-oedema treatment will be implemented without impairing overall wound healing.

Surgical risks: As a surgical patient undergoing haemorrhoidectomy, you remain exposed to standard surgical risks including bleeding, surgical-site infection and anaesthetic complications. These risks exist for all patients receiving this operation.

Mitigation measures will be implemented to minimise risk:

1. Full disclosure of potential risks so you can give truly informed voluntary consent.

2. Rigorous monitoring procedures for timely identification and management of adverse events.

3. Data encryption and de-identification to protect your information security.

Free-of-Charge Services and Compensation

Routine clinical costs related to anaesthesia and surgery are at your expense. Questionnaires and rating scales (including QoR-15) required for this study are provided free of charge by the research group. Upon completion of study participation, you will receive one free post-discharge health-recovery consultation.

Compensation for Research-Related Injury

If your health is harmed as a consequence of study participation, please notify investigators promptly, and appropriate medical measures will be implemented to protect your wellbeing.

If harm is confirmed by formal appraisal to be causally related to research procedures,

compensation will be provided in accordance with relevant national laws and regulations.

Voluntary Participation and Right to Withdraw

Your participation is entirely voluntary. You may refuse enrolment without penalty and without compromising present or future medical services. Even after consenting, you may withdraw from the study at any time without giving any reason; withdrawal will not affect standard clinical care. If you decide to discontinue participation, please inform your study physician, who may provide health-related suggestions.

Any new information that may alter your willingness to stay in the study will be communicated to you in a timely manner.

Premature termination of your individual participation may occur if: postoperative insufficient arousal or delirium prevents assessment; severe haemodynamic or respiratory compromise occurs; or other circumstances make continuation inappropriate in the investigator's judgment.

Tongliao People's Hospital or higher-level regulatory authorities may suspend or terminate the whole study. You will be notified promptly, and your study physician will advise you on subsequent clinical management.

After withdrawal, a final safety follow-up may be performed; you retain the right to refuse this follow-up. Please return any unused study medication to your study physician. Should new health- or rights-relevant information emerge after your withdrawal, you may be contacted again.

After withdrawal, your research-related records will be securely retained until scheduled destruction; no further use or disclosure of identifiable data will occur.

Confidentiality of Research Data

Your research records will be kept confidential as required by applicable law. Chinese legislation safeguards privacy, data security and authorised data access. Except as required by law, your name, ID number, address, telephone number and other personally-identifiable information will not be disclosed outside Tongliao People's Hospital. Data transmitted externally will be coded using a unique subject identifier stored securely at Tongliao People's Hospital. Nevertheless, study records may be reviewed by health authorities, government agencies and ethics-committee representatives to verify study compliance. When study results are published in scientific journals or presented at conferences, your personal identity will remain undisclosed.

SIGNATURE PAGE OF INFORMED CONSENT FORM

Investigator's Statement

I have explained to this subject the background, objectives, procedures, risks and benefits of the clinical study entitled "Liposomal Bupivacaine versus Ropivacaine Hydrochloride for Post-Operative Analgesia Management after Haemorrhoidectomy". Sufficient time was allowed for reading this document and for consultation. All questions raised by the subject have been answered. I have informed the subject whom to contact for study-related questions (Wang Xiuli) and whom to contact for rights- and welfare-related issues (Medical Ethics Committee of Tongliao People's Hospital), with accurate contact information provided. I have explained that the subject may withdraw from the trial at any time without giving reasons. A signed copy of this informed consent form will be provided to the subject.

Investigator Signature:

Date:

Contact Information:

Subject Statement

I have been informed of the research background, purpose, procedures, risks, and benefits of the clinical study titled "Liposomal Bupivacaine versus Ropivacaine Hydrochloride for Pain Management after Hemorrhoidectomy". I have been given adequate time and opportunity to ask questions, and I am satisfied with the responses provided.

I have also been informed who to contact if I have questions, concerns, suggestions, or require further information about the study, or if I wish to offer assistance to the research.

I have read this informed consent form and agree to participate in this study. I understand that I may withdraw from this study at any time during the study period without providing any reason.

I have been advised that I will receive a copy of this informed consent form bearing both my signature and the investigator's signature.

Subject Signature:

Date: June

Contact Information:

(If the subject lacks or has insufficient capacity to provide informed consent, the following section shall be added or substituted.)

Legal Guardian Signature:

Relationship to Subject:

Date:

Contact Information:

Impartial Witness Signature:

Date: