PROTOCOL

Obturator Nerve Block and Pericapsular Nerve Group Block for Preventing Obturator Nerve Reflex: A Randomized Controlled Trial

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Block and Pericapsular Nerve Group Block for Preventing Obturator Nerve Reflex: A Randomized Controlled Trial

1 Research background Bladder cancer is a common urological tumor in clinical practice. Transurethral resection of bladder tumor (TURBT) is a widely used surgical treatment for bladder cancer, offering advantages such as minimal invasiveness and high patient acceptance.

TURBT is commonly performed under spinal anesthesia. The obturator nerve is located near the inferolateral wall of the bladder and the bladder neck within the pelvis. During transurethral resection of tumors in these areas, the electrical current can easily pass through the bladder wall, directly stimulating the obturator nerve, leading to an obturator nerve reflex in the patient.

It has been reported that during TURBT involving the lateral bladder wall without ONB, 40% of patients experienced sudden thigh movement, and 5.7% had bladder perforation. A retrospective study compared the recurrence rates of patients with lateral bladder wall tumors undergoing TURBT with or without ONB, showing that ONB prolonged the average time to bladder tumor recurrence by 7.8 months and 15 months, respectively.

The obturator nerve originates from the anterior branches of the second, third, and fourth lumbar nerves. It runs along the lateral wall of the lesser pelvis and, after passing through the obturator canal, immediately courses between the pectineus muscle and the external obturator muscle, extending to the anterior thigh. The obturator nerve divides into anterior and posterior branches during its course. In cadaveric studies, the bifurcation of these two major branches was identified as occurring within the pelvis (23.22%), within the obturator canal (51.78%), or in the medial thigh (25%) .

The nerve passes through the obturator foramen into the thigh, where it divides into anterior and posterior branches. After exiting the obturator foramen, it extends deeper into the pectineus muscle. Typically, the anterior branch runs along the fascial plane between the adductor longus and adductor brevis, while the posterior branch runs between the adductor brevis and adductor magnus.

The pericapsular nerve group (PENG) block is a novel ultrasound-guided nerve block technique. By injecting local anesthetic between the psoas major muscle and the pubic bone, it provides analgesia for patients with hip fractures.

The obturator nerve (ON) and accessory obturator nerve (AON) run between the pectineus muscle and the external obturator muscle. Injecting local anesthetic between the pectineus muscle and the superior pubic ramus can theoretically block both the obturator nerve and the accessory obturator nerve through diffusion.

In a 2022 study, researchers simulated a PENG block by injecting 20 mL of methylene blue into 18 hip joint specimens. The cadavers were then dissected to document the presence and dye staining of the femoral, lateral femoral cutaneous, obturator, and accessory obturator nerves, as well as the articular branches of the femoral, obturator, and accessory obturator nerves. The results indicated that the PENG block can successfully block the main trunk of the obturator nerve .

The primary reason for obturator nerve blockade may be that the iliopubic fascia forms the medial end of the iliac fascia, acting as a barrier to prevent the local anesthetic from further medial spread to reach the obturator nerve within the deep pectineus muscle. However, the iliopubic fascia has a relatively short course in the cranio-caudal direction, suggesting that using a high volume of local anesthetic with a PENG block could potentially result in obturator nerve blockade below the pubis .

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2 Study objective and study endpoint

Study on the Efficacy and Safety of PENG Block in Preventing Obturator Nerve Reflex During Transurethral Resection of Bladder Tumors: A Single-Center, Randomized, Single-Blind, Parallel-Controlled Trial.

2.1 Study Purpose

2.1.1 Main study objective:

Evaluate the effectiveness of the pericapsular nerve group (PENG) block in preventing obturator nerve reflex during transurethral resection of bladder tumors.

2.1.2 Secondary study objective:

Evaluate the safety of the pericapsular nerve group (PENG) block in preventing obturator nerve reflex during transurethral resection of bladder tumors.

2.2 Study endpoint

2.2.1 Primary study endpoints

Percentage reduction in adductor muscle strength at 5, 10, 15, 20, 25, 30 minutes, and 3 hours post-administration.

2.2.2 Secondary study endpoints

2.2.2.1 Effectiveness study endpoint

1) Presence of obturator nerve reflex during surgery.

2）Duration of the surgery

3）Surgeon satisfaction and patient satisfaction.

2.2.2.2. Safety study endpoint

1）Incidence of adverse reactions such as local anesthetic toxicity and nerve injury post-administration.

2）Procedure time and number of needle passes.

3. Expected results

Pericapsular nerve group (PENG) block is effective and safe in preventing obturator nerve reflex during transurethral resection of bladder tumors.

4. Design and method of the study

This clinical study uses a single-center, randomized, single-blind, parallel controlled trial design, divided into screening period, treatment period and follow-up periods.

4.1.1 Screening period:

Patients undergoing transurethral resection of bladder tumors signed informed consent forms for enrollment. Subjects who met all inclusion criteria and did not meet any exclusion criteria were randomized in a 1:1 ratio to the experimental and control groups, either one day before surgery or on the day of surgery.

4.1.2 Treatment Period

Upon entering the operating room, HR, BP, ECG, and SpO2 were monitored. Intravenous access was established, and oxygen was administered.Patients were randomly divided into two groups using a random number table: the pericapsular nerve group (PENG) block group (P group) and the obturator nerve block group (O group).

In the P group, patients were placed in the supine position, and the inguinal region was exposed, followed by routine disinfection and draping. A convex ultrasound probe (frequency 2-5 MHz) was positioned at the patient's inguinal ligament, with one end directed toward the anterior inferior iliac spine (AIIS), clearly visualizing the bony prominences of the iliopubic eminence and the AIIS. An out-of-plane technique was used, with the needle tip directed medially toward the pectineus muscle. Care was taken to avoid the femoral artery, vein, and nerve during needle insertion. Once the

needle tip reached the space between the pectineus muscle and the pubic bone, and after confirming no blood upon aspiration, 30 ml of 0.375% ropivacaine was injected.
In the O group, patients were placed in the supine position, with the affected thigh abducted and externally rotated. The ultrasound probe was positioned at the inguinal ligament and moved medially to locate the adductor muscles and pectineus muscle. Care was taken to avoid the femoral artery and vein, and the obturator nerve and fascial planes of the muscle layers were identified step by step. The needle was inserted parallel to the long axis of the probe. After confirming no blood upon aspiration, 15 ml of 0.375% ropivacaine was injected into the fascial plane between the adductor brevis and adductor magnus, as well as into the midportion of the adductor longus and adductor brevis muscles.
Anesthesia induction was performed with propofol at 1-2 mg/kg, sufentanil 10 μg, and remifentanil 1.5 μg/kg, followed by mask ventilation for 5 minutes. A laryngeal mask was inserted for mechanical ventilation. The ventilation mode selected was pressure-controlled with volume guaranteed, with FiO2 at 45%, tidal volume (VT) 6-8 ml/kg, PEEP 4-6 cmH2O, Iratio 1:2, and respiratory rate (RR) 12-20 breaths per minute. Anesthesia maintenance was achieved with a continuous infusion of propofol at 4-6 mg/kg/h and remifentanil at 0.1–0.3 μg/kg/min.
4.1.3 Follow-up period
Neurological complications, hematoma at the puncture site, patient satisfaction, and doctor satisfaction.
5.0 Study the implementation process
After entering the room, intravenous access was established, and routine monitoring of ECG, NBP, and SpO2 was performed. Based on group assignment, the same physician experienced in nerve blocks performed either the obturator nerve block or the pericapsular nerve group (PENG) block. Anesthesia was induced and maintained according to a standardized protocol.The same anesthesiologist, who was unaware of the group assignments, collected various study parameters and data.
6. Subject recruitment and protective measures
6.1 Inclusion criteria
Aged 18 years or older：scheduled for TURBT for unilateral bladder tumor：able to understand and provide informed consent.
6.2 Exclusion criteria
Patients who refuse or are unable to provide informed consent; allergic to local anesthetics, insensitive to propofol or general anesthetics; pregnant women; severe liver dysfunction; evidence of infection at or near the proposed puncture site; any sensory or motor impairment of the lower limbs; recent (within 6 months) lower limb joint replacement surgery.
6.3 Exit criteria
Patients may withdraw their informed consent and withdraw from the trial at any time.
The investigator may decide on the subject to terminate the withdrawal from the study in the following circumstances
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1) Any medical condition occurring in the study may lead to the risk of continuing the study subjects;
2) Unable to complete the trial according to the protocol for various reasons；
3) The researcher judges other situations that should withdraw from the trial.

7 Informed consent

7.1 The Informed Consent Form

The informed consent was in accordance with the ethical principles outlined in the Declaration of Helsinki.The informed consent form detailed the study protocol and process, and fully explained the risks of the study.

The informed consent form also states that the records of the individual identity must be kept confidential, but the research team and regulators can access the subject information.

7.2 Informed consent process and recording

Informed consent begins before the individual consent to participate in clinical studies and continued throughout the course of the clinical study.

7.3 Confidential

Personal patient information will be given as confidential information.All patient data obtained from the patient cases will be kept as confidential.Patients will be identified by their name acronym and the numbers provided at the time of study inclusion.Patients or their families will be aware of the anonymity of the data and their right to protect their privacy.However, it is also important to understand the fact that the data will be submitted to the subject responsible unit or the government management authority, and may also be submitted to institutions such as the Ministry of Health for inspection and evaluation.The participating physician will keep a list of patient personal data (patient data and corresponding patient names) for confirmation of the record.

8.Quality control and quality assurance

8.1Qualification of research unit and researcher qualification

The research unit shall have the experience in drug research, the facilities and conditions of the department where the project belongs shall meet the needs of safe and effective clinical research, and the researchers shall have the professional expertise, qualifications and ability to undertake the clinical research, and shall be trained in GCP regulations.

8.2Training of the researchers

Before the start of the study, the research leaders of each center should organize the researchers to study the program, and only the researchers who have passed the program training can participate in the study to ensure that the researchers have a consistent understanding of the protocol.For important assessment scales, relevant personnel in the participating centers need systematic training and even obtain corresponding qualification certificates.

8.3Surveillance of clinical trials

A hospital ethics committee and institutional review board may conduct a systematic review of the clinical trial-related activities and documents, to evaluate whether the trial was conducted in accordance with the trial protocol, SOP, and relevant

regulations, and whether the trial data are timely, true, accurate, and complete records.The audit should be performed by those who do not directly involve the clinical trial.

9.Organization and management of the research

9.1Change of the scheme

All additional or referenced appendices are integral parts of the scheme.No one shall make any modifications or revisions to any part of the research protocol, as signed by the investigator and the principal of the project, unless these changes or revisions have been fully discussed.And through the unanimous consent of the researcher and the subject leader.Any agreed modification will be recorded and will be signed by the investigator and the project leader

The case is filed together.

9.2Retention of the records

The investigator shall keep all the detailed original documents of the subject, and record the trial process, medication status, laboratory examination data, safety data and efficacy assessment in the case report form. The recorded data shall be complete, timely and clear.The original documents and medical records should be clear, detailed and easily identified by those participating in this clinical trial. The case report form and the original files can only be modified by the investigator.No modification to the case report form and the original file shall smear the original data off.The correct way to modify is to line the original data, and then write the modified data next to the original data, and sign the date and the name of the modification.Test data shall be retained until 5 years after the termination of the test.

9.3Early termination of the study

The leader of the project decides to stop or interrupt the study in advance in the case of force majeure, and should inform the doctors involved in the study in writing.Similarly, any participating unit that decides to withdraw from the study for any reason should also notify the project leader in written form.

9.4Research, supervision and inspection

9.4.1Research supervision

Inspectors must follow the drug clinical trial quality management specification (GCP) and standard operation procedures (SOP), visit the research unit regularly or according to the actual situation, supervise the clinical trial work and progress, check, confirm all data records and reports, correct and complete, consistent with the original data, ensure the clinical trial in accordance with the clinical trial protocol, the researchers should actively cooperate with the inspectors.The specific contents of the inspector include:

A) Ensure before the test that the test undertaking unit has appropriate conditions, including staffing and training, complete laboratory equipment and good operation, various inspection conditions related to the test, and estimated sufficient quantity All the participants were familiar with the requirements in the test protocol;

B) Monitor the implementation of the trial protocol during the trial, confirm that the informed consent of all subjects is obtained before the trial, understand the enrollment rate of the subjects and the progress of the trial, and confirm that the selected subjects

are qualified;
C) Confirm that the records and reports of all data are correct and complete, and that all case report forms are entered correctly and consistent with the original data.All errors or omissions have been corrected or indicated, signed and dated by the Investigator.
D) Verify that all adverse events are recorded, and that serious adverse events shall be reported and recorded within the specified time;
E) Clearly and truthfully record the failed visits, unconducted tests, and undone checks should be made, and whether the errors and omissions should be corrected;
F) The written inspection report shall be completed after each visit, which shall state the date, time, name of the inspector, findings of the inspection, etc.
9.4.2 On-site inspection
The responsible unit may conduct an on-site inspection of the research at a clinical research institution.The audit includes the required test documents, records of the informed consent process, and the consistency of the eCRF and the original documents.But also the content and scope of the inspection can be increased according to the situation.The investigator agrees to participate at a reasonable time and in a reasonable manner.
10.Investigators' responsibilities
10.1Participating physician responsibilities
The participating physicians will implement the study following the study protocol and confirm the accuracy of the data entered.The participating physicians should be responsible for obtaining written signed informed consent for data collection from the study subjects.
10.2Responsibility of the project leader
The project leader takes all reasonable steps and provides sufficient resources to ensure the implementation of the research, mainly involving the following aspects:
A) Ensure that the study complies with relevant national and local regulations, including ethical requirements, patient data protection regulations, etc.
B) Ensure the effectiveness of quality control and analysis of research results.
11.Results sharing
The intellectual property rights, trial data and research results related to this anatomical study are jointly owned by the Nanjing First Hospital and the Department of Anesthesiology, and the University and the Anatomy Teaching and Research Section of Nanjing Medical University.
The intellectual property rights, trial data and research results related to this clinical study are owned by Nanjing First Hospital and the Department of Anesthesiology.
12.Data analysis
Data collection: It was collected by the same anesthesiologist who did not know the grouping situation.
Statistical analysis was performed using SPSS 22.0 software. Measurement data were expressed as mean ± standard deviation (X±s), and comparisons between groups were conducted using the paired t-test. Categorical data were compared using the chi-square (χ^2) test, and ordinal data were compared using the rank-sum test. A

P-value of <0.05 was considered statistically significant.

13. Ethics principles and requirements for clinical research Clinical research will follow the world medical congress of the declaration of Helsinki and the national health and family planning commission of the People's Republic of China involving human biomedical research ethics review method and other relevant provisions, the specific implementation of informed consent, the privacy protection, research free and compensation, risk control, special subject protection and research related damage compensation principles and requirements.The clinical study was performed before the ethics committee approved the trial protocol.Before each subject is enrolled in the study, the investigator has the responsibility to present the subject or his legal agent about the purpose, procedures of the study and possible risks, and sign a written informed consent form that their participation in the clinical study is completely voluntary, that they may refuse to participate or withdraw from the study at any time at any stage of the trial without discrimination and retaliation, and their medical treatment and interests are not affected.The informed consent form should be retained as a clinical research document for future reference to effectively protect the subjects' personal privacy and data confidentiality.