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Epidural morphine combined with single-injection femoral nerve block for postoperative analgesia in patients after total knee arthroplasty: a randomized controlled trial V.2

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ABSTRACT

Total knee arthroplasty (TKA) is an important therapy for patients with serious knee osteoarthritis in order to improve quality of life and relieve pain. But a large number of patients who undergo this surgery experience moderate to severe postoperative pain. Previously, the investigators used single femoral nerve blockade combined with patient-controlled intravenous analgesia for postoperative analgesia for patients after TKA. Although this method provides acceptable analgesia, the incidence of opioid-associated side effects is relatively high. Low-dose epidural morphine is commonly used in postoperative analgesia after cesarean section, and the effect of single dose morphine lasts more than 20 hours, with low incidences of itching, nausea, vomiting, and respiratory depression. The investigators hypothesize that, for patients undergoing TKA, the addition of low-dose epidural morphine to single femoral nerve block and intravenous opioids can improve the postoperative analgesia, reduce the consumption of intravenous opioids and decrease opioid-associated side effects.

EXTERNAL LINK

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DOCX

R1-S1 Protocol..docx

MATERIALS TEXT

Participants

Inclusion criteria: Adult patients (age of 18 years or older) who are scheduled to undergo unilateral TKA under combined spinal-epidural anesthesia.

Exclusion criteria:

(1) age higher than 90 years;
(2) presence of any contraindication to neuraxial anesthesia or peripheral nerve block;
(3) use of opioid analgesics during the last month;
(4) unable to understand Numeric Rating Scale for pain evaluation or existence of language barrier;
(5) severe renal insufficiency (requirement of renal replacement therapy);
(6) history of asthma;
(7) American Society of Anesthesiologists (ASA) classification of grade IV or higher.

BEFORE STARTING

Total knee arthroplasty is an important therapy for patients with later-stage knee osteoarthritis to relieve pain and improve quality of life. However, many patients suffer from moderate to severe postoperative pain that impede them from participating early physical therapy and recovering joint function. In addition, severe postoperative pain also contributes to immobility-related complications like deep vein thrombosis and delay hospital discharge. Although the analgesic techniques have been greatly improved, the effect is far from optimal. Femoral nerve block is commonly used for analgesia after open knee surgery. But femoral nerve block alone is not satisfactory because of limited blocking range and duration; therefore, it is usually combined with supplemental analgesics which may produce opioid-associated side effects.

Low-dose epidural morphine is commonly used for analgesia after cesarean section. The effect of single dose morphine lasts more than 20 hours, with low incidences of itching, nausea, vomiting, and respiratory depression. We hypothesized that, for patients undergoing TKA, combined use of low-dose epidural morphine and single femoral nerve block could improve the effect of postoperative analgesia, reduce the consumption of intravenous opioids and decrease opioid-associated side effects. The purpose of this study is to compare the analgesic effect of low-dose epidural morphine combined with single-injection femoral nerve block and single-injection femoral nerve block alone in patients following TKA.

Enrollment

1 Patients will be screened the day before surgery. And eligible patients will be enrolled for their consent in advance and written informed consent will be signed.

Randomization

2 This is a randomized, double-blind, and placebo-controlled one-center trial. The random numbers were generated in a 1:1 ratio with a block size of 4 by an independent biostatistician using the SAS statistical package version 9.3 (SAS Institute, Cary, NC, USA). Each enrolled patient will be assigned a number according to the sequence of recruitment. The study drugs, either 2 mg morphine in 5 mL normal saline or 5 mL normal saline, will be prepared according to the randomization results by a study coordinator who will not participate in the rest of the study. The prepared drugs will be contained in 5 mL syringes with same appearance, labeled with the number of recruitments, and provided to the anesthesiologists taking care of the enrolled patients. The results of randomization and the preparation of study drugs will be recorded and sealed in sequentially numbered letters and stored at the site of investigation until the end of the study.

Intervention and anesthesia management

3 Combined spinal (with 0.5% hyperbaric bupivacaine) and epidural (with 2% lidocaine) anesthesia will be performed for all patients. The dosage of local anesthetics (either spinal bupivacaine or epidural lidocaine) will be determined by the anesthesiologists. Intraoperative sedation will be provided with dexmedetomidine infusion (a loading dose of 0.4 μg/kg in 10 minutes, followed by a 0.2 μg/kg/h infusion) which will be started once patients become hemodynamically stable after spinal anesthesia, and stopped before the end of surgery. The study drugs (morphine for patients in the epidural morphine [EDMO] group and normal saline for those in the control [CTRL] group) will be administered at the end of surgery through the indwelling epidural catheter which will be removed afterwards.

4 Patients will be transferred to the post-anesthetic care unit (PACU), where single-injection femoral nerve block will be performed with 20 mL of 0.5% ropivacaine under the guidance of ultrasonography and a nerve stimulator. A patient-controlled intravenous analgesia (PCIA) pump will also be provided, which is established with 100 mL of 0.5 mg/mL morphine and programmed to deliver a 2 mL bolus with a lockout interval of 8–10 min and a background infusion of 0.5 mL/h. The PCIA pump will be stopped at 48 hours after surgery. If the morphine solution in the pump is exhausted before that time, supplemental morphine of same concentration will be provided to ensure a 48-hour postoperative patient-controlled analgesia.

Outcome assessment and follow-up schedule

5 After obtaining the written informed consents, detailed baseline data including demographic characteristics, diagnosis, comorbidities, current medication, NYHA classification, American Society of Anesthesiologists (ASA) classification, history of previous surgery and anesthesia, as well as important laboratory test results will be collected.

6 Intraoperative data including duration of anesthesia and surgery, name of surgery, types and doses of anesthetic drugs, and fluid balance will be recorded. After surgery, patients will be monitored in PACU for at least 30 minutes. Motor blockade of the lower limbs will be estimated using a modified Bromage scale (0 = no motor block, able to lift extended limb off the bed; 1 = partial block, able to flex/extend the knee and ankle; 2 = partial block, only plantar flexion of the ankle possible; 3 = complete block, no voluntary movement of the limb) at PACU arrival and 30 minutes.

7 After surgery, investigators will visit patients at 6, 12, 24, 36, and 48 hours after surgery (1 hour earlier or later is allowed). The severity of pain at rest and with movement will be assessed with the numerical rating scale (NRS, an 11-point scale where 0 = no pain and 10 = the most severe pain). Motor blockade of the lower limbs will be estimated using a modified Bromage scale. The numbers of required and given bolus injections by the PCIA pumps between the neighbouring time-points will be counted. The occurrence of side effects (nausea, vomiting, pruritus, and dizziness), the uses and dosages of other analgesics, the volume of drainage, and the requirement of blood transfusion within 48 hours will be recorded. The score of patients' satisfactions (1 = poor, 2 = fair, 3 = good, 4 = excellent) will be evaluated

at 48 hours after surgery. Other postoperative date including time to ambulation, length of postoperative hospital stays, occurrence of complications within 30 days, and 30-day mortality after surgery will be documented.

8 At 30 days after surgery, the quality of life will be assessed with 12-item short-form; the severity of arthritic symptoms will be assessed with WOMAC osteoarthritis index. 30-day followed-up will be performed by face-to-face interview, when patients come back to the hospital for a re-examination.