The Effect of Esketamine as an Adjuvant for Adductor Canal Block on Postoperative Pain in Patients Undergoing Arthroscopic Knee Surgery: A Randomized Controlled Trial

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AIM: To evaluate the efficacy of esketamine as an adjuvant for adductor canal block (ACB) in alleviating postoperative pain in patients undergoing arthroscopic knee surgery.

METHODS: This single-center prospective randomized controlled trial enrolled 100 patients who underwent arthroscopic knee surgery at The General Hospital of Northern Theater Command of the Chinese People's Liberation Army from October 2022 to March 2023. Patients were randomly and evenly divided into four groups. Patients in the R group received ACB of 0.375% ropivacaine 20 mL before awakening, while patients in the L, M, and H groups received 0.375% ropivacaine 20 mL mixed with 20 mg, 30 mg, and 40 mg of esketamine respectively.

RESULTS: The sensory block duration of the M and H groups was significantly longer than that of the R group ($p = 0.042$ and $p = 0.003$, respectively). Immediately and 8 hours after surgery, the resting and motor pain scores of the M and H groups were significantly reduced ($p < 0.05$), while the L group also showed a significant decrease at 8 hours after surgery ($p = 0.003$ and $p = 0.032$, respectively). Immediately after surgery, subjects of the H group were more deeply sedated than those of both the R and L groups ($p = 0.039$ and $p = 0.041$, respectively). However, the recovery quality of group H one day after surgery was worse compared with the other three groups ($p < 0.001$, $p = 0.001$ and $p = 0.030$, respectively).

CONCLUSIONS: Compared to the use of ropivacaine alone, esketamine adjuvant can prolong the duration of ACB and reduce early postoperative pain. However, high-dose esketamine affects the quality of postoperative recovery and increases the risk of adverse effects. Clinical Trial Registration: Chinese Clinical Trial Registry (ChiCTR2200065236).

Keywords: esketamine; adductor canal block; arthroscopic knee surgery; postoperative analgesia; recovery quality

Introduction

Knee arthroscopy, as a classic surgical auxiliary measure, has a wide range of indications and significant advantages such as minimal trauma, minimal bleeding, precise therapeutic effect, and fast recovery [1]. However, the accompanying postoperative pain, which is typically of moderate to severe levels, often hampers quick recovery in patients. To address this thorny issue, numerous analgesic schemes have been reported in the past few decades, including intra-articular injection, the use of non-steroidal anti-inflammatory drugs, and nerve block [2–4].

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The nerves innervating the knee joint can be mainly divided into anterior and posterior groups, namely the femoral nerve and its branches, and the sciatic nerve and its branches, respectively. In addition, secondary nerves such as the obturator nerve also innervate some areas of the knee joint [5]. Therefore, various nerve block techniques, including femoral nerve block, sciatic nerve block, obturator nerve block, saphenous nerve block, and patellar nerve block, have been reported and applied in knee arthroscopic surgery [6–9]. The main target of adductor canal block (ACB) is the saphenous nerve, which is diffused within the adductor canal through local anesthetics to block other nerves. Compared to traditional femoral nerve block, ACB can preserve quadriceps femoris muscle strength while inducing a similar analgesic effect as the femoral nerve block [10,11].

To reduce the dosage of local anesthetics and prolong the analgesic duration, adjuvants are often mixed with local anesthetics during regional anesthesia. Regarding ACB inducement, drug regimens mixed with clonidine, dexamethasone, dexmedetomidine, and butorphanol as adjuvants have been reported in the literature [12–15]. Ketamine is a

non-specific blocker of N-methyl-D aspartic acid (NMDA) receptors, and can stimulate opioid receptors to exert analgesic effects. Ketamine, when used as an adjuvant for intrathecal bupivacaine, has been reported to achieve faster onset time and longer block duration [16]. However, the effectiveness of ketamine as an adjuvant in nerve block is still controversial [17–20].

The purpose of this study was to evaluate the efficacy of esketamine as an adjuvant for ACB in reducing postoperative pain in patients undergoing arthroscopic knee surgery, and to provide the evidence-based medical basis for the clinical application and ongoing study of adjuvants.

Methods

Study Design

This study was approved by the Medical Ethical Committee of the General Hospital of Northern Theater Command Y(2022)093 and registered at the China Clinical Trial Registration Center (ChiCTR2200065236). The drugs under investigation were administered only after obtaining informed consent from the patients or their family members. The trial was conducted in adherence to the principles of the Declaration of Helsinki and reported following the Consolidated Standards of Reporting Trials (CONSORT) 2013 guidelines [21].

Sample Size Determination

According to preliminary unpublished research data, the standard deviation of pain scores, determined using Visual Analogue Scale (VAS), in the control group is about 2.0, and the expected difference in mean pain scores between groups is approximately 1.5. A calculation using the formula $N = 2 (Z\alpha + Z\beta) 2\sigma 2/d2$ ($\alpha = 0.05$, $\beta = 0.2$, $\sigma = 2.0$, $d = 1.5$) determined that 23 cases were required per group. Considering a 10% dropout rate, we planned to enroll 25 cases in each group, totaling 100 cases in four groups investigated in this trial (see the ACB section for details about grouping).

Population

The study recruited patients who underwent knee arthroscopic surgery under general anesthesia at the General Hospital of Northern Theater Command of the Chinese People's Liberation Army from October 2022 to March 2023. Only patients meeting the following inclusion criteria were included: (1) age >18 years; (2) body mass index (BMI) <28 kg/m^2; and (3) American Society of Anesthesiologists (ASA) classification system grade I or II. Individuals with the following conditions were excluded: (1) known drug allergy or hypersensitivity; (2) peripheral nerve disorder or injury; (3) chronic pain history; (4) severe cardiovascular, respiratory, hematological, endocrine disorders or hepatic/renal dysfunction; (5) risk of hypertension, intraocular hypertension (such as glaucoma), intracranial hypertension; (6) surgery or investigational drugs use within one week before operation; (7) communication difficulties (such as language, visual or hearing impairment), concomitant neurological or psychiatric disorders; and (8) refusal to sign the informed consent form. Patients enrolled in the study were randomly and evenly assigned to four groups using a random number table, and interventions were implemented on the subjects according to the assigned group.

Perioperative Period and Anesthesia Management

Patients routinely fasted for 8 hours and refrained from drinking liquids for 6 hours prior to surgery, and no preoperative medication was administered to any patients. Upon arrival in the operating room, a peripheral intravenous cannula was inserted, and non-invasive monitoring of arterial blood pressure (BP), heart rate (HR), pulse oxygen saturation (SpO_2), and body temperature was initiated. Baseline preoperative HR, BP, and SpO_2 were recorded for each patient. After verifying patient information, anesthesia induction was performed with 0.2–0.5 μg/kg fentanyl (AB40402131, Humanwell Pharmaceutical Co., Ltd., Yichang, China), 2.0 mg/kg propofol (22205101, Jiabo Pharmaceutical Co., Ltd., Qingyuan, China), and 0.6 mg/kg rocuronium bromide (EA2213, Xianju Pharmaceutical Co., Ltd., Taizhou, China). Proper oxygenation was ensured, and loss of consciousness following anesthesia was confirmed by the absence of corneal and palpebral reflexes, after which an oropharyngeal airway was inserted. Anesthesia was maintained using controlled ventilation with a tidal volume of 6–8 mL/kg and a respiratory rate of 12–14 bpm, with a Fraction of lnspiration O_2 (FiO_2) of 50%. Anesthesia maintenance involved continuous infusions of 0.1–0.3 μg/(kg·min) remifentanil (AC2070191, Humanwell Pharmaceutical Co., Ltd., Yichang, China), 2–4 mg/(kg·h) propofol, and inhalation of 0.7–1.0 MAC sevoflurane (Hengrui Pharmaceutical Co., Ltd., Shanghai, China). The specific dosages of all drugs were adjusted by a senior anesthesiologist based on the intraoperative phase and patient response. The total doses of fentanyl, remifentanil, propofol, and sevoflurane administered during anesthesia were recorded for each patient. Intraoperative blood pressure was maintained within ±20% of the baseline using a continuous infusion of 0.02% norepinephrine (2205006, Grand Pharmaceutical Group Co., Ltd., Wuhan, China). If a patient's blood pressure dropped by more than 20% from baseline or if systolic blood pressure was less than 90 mmHg during surgery, a single intravenous dose of 6 mg ephedrine (220501, Dongbei Pharmaceutical Group Company Shenyang No.1 Pharmaceutical Co., Ltd., Shenyang, China) was administered. If intraoperative blood pressure increased by more than 20% above baseline, 10–25 mg urapidil (2203122, Takeda Austria GmbH, Linz, UA, Austria) was administered. If the HR decreased below 45 bpm, 0.3–0.5 mg atropine (220301004, Changjiang Pharmaceutical Co., Ltd., Wuhu, China) was administered. If the HR increased above 100 bpm, 0.5 mg/kg esmolol (2H0212304, Qilu Pharmaceutical Co., Ltd., Jinan, China) was administered, with repeat doses given as necessary. The usage of

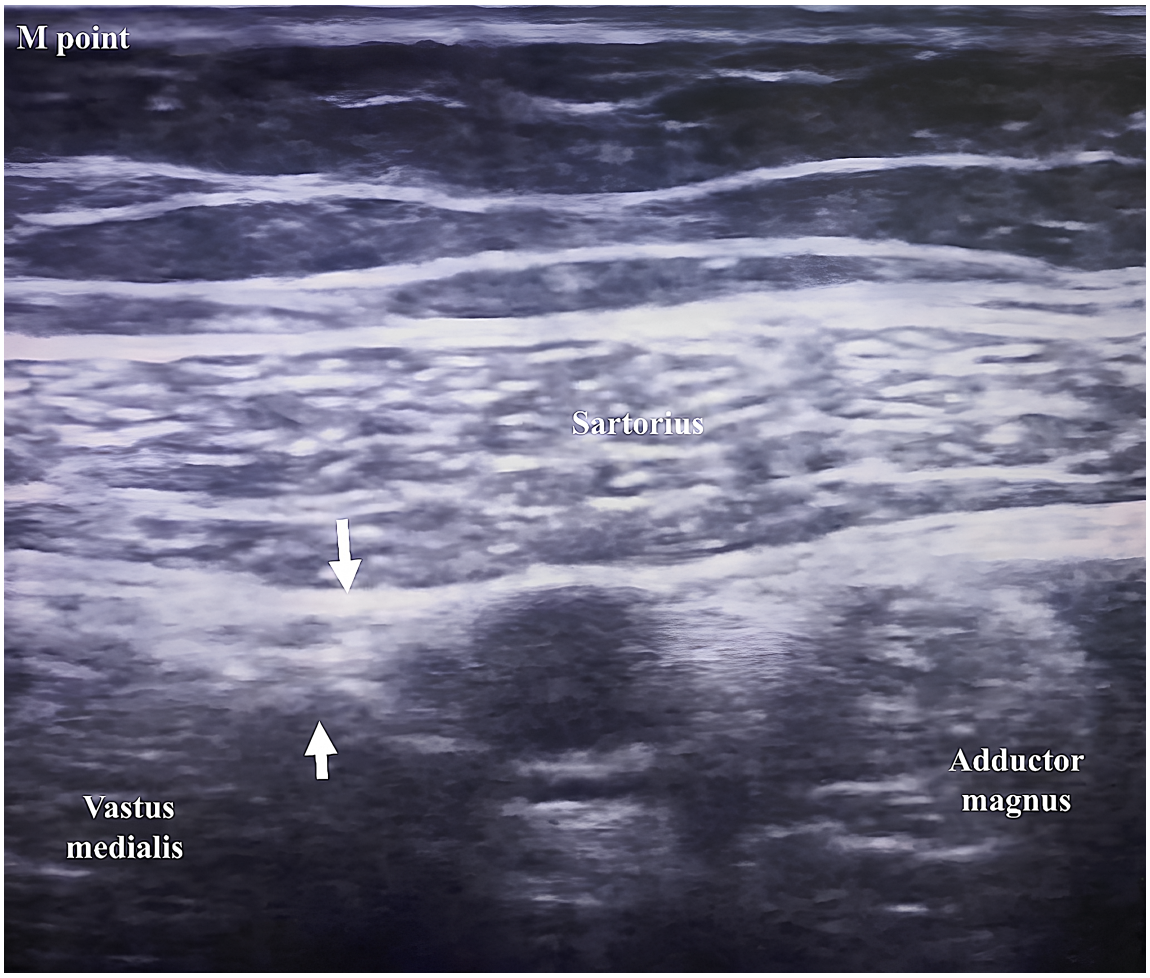

Fig. 1. Ultrasound scan of the structures within the adductor canal. The arrows point to the saphenous nerve clusters.

these additional medications was recorded, and the proportion of patients receiving ephedrine, urapidil, atropine, or esmolol was documented.

Intraoperative blood loss was estimated and recorded for each patient. The duration of surgery was also recorded, defined as the time from the first surgical incision to the completion of the procedure. The inhalation of sevoflurane was stopped 30 minutes before the end of the operation, and the infusion rates of propofol and remifentanil were adjusted accordingly. At the end of the surgery, the propofol infusion was stopped, and the ultrasound-guided ACB was performed as previously described [21]. After completing the blockade, the remifentanil infusion was stopped, and patients were transferred to the post-anesthesia care unit (PACU). The oropharyngeal airway was removed once patients regained full consciousness, the ability to swallow and cough, and resumed normal breathing. These additional perioperative variables—including baseline vital signs, intraoperative anesthetic dosages, duration of surgery, blood loss, and usage of additional medications—were collected to assess and control for factors that could influence postoperative analgesia outcomes. This comprehensive data collection helps a more accurate comparison between groups and ensures that any differences in postoperative pain and recovery are attributable to the interventions studied rather than confounding variables.

Adductor Canal Block

After the surgery, all patients were subjected to an ultrasound-guided ACB before awakening to ensure optimal analgesia. Using strict aseptic techniques to prevent infection, an in-plane ultrasound-guided approach was employed. A high-frequency linear ultrasound probe was placed at the mid-thigh level to precisely locate the adductor canal. The probe was moved to a point where the junction of the sartorius, adductor magnus, and vastus medialis muscles could be identified. The femoral artery and saphenous nerve clusters were visualized beneath the sartorius muscle (Fig. 1) to confirm the correct site for injection. The needle was cautiously advanced through the membrane of the sartorius into the adductor canal, ensuring minimal tissue trauma and avoiding vascular puncture. Local anesthetic solutions were prepared immediately before administration. Patients in the ropivacaine group (R group) received 20 mL of 0.375% ropivacaine, while patients in the low-dose, middle-dose, and high-dose esketamine groups (L, M, and H groups, respectively) received 20 mL of 0.375% ropivacaine mixed with 20 mg, 30 mg, and 40 mg of esketamine,

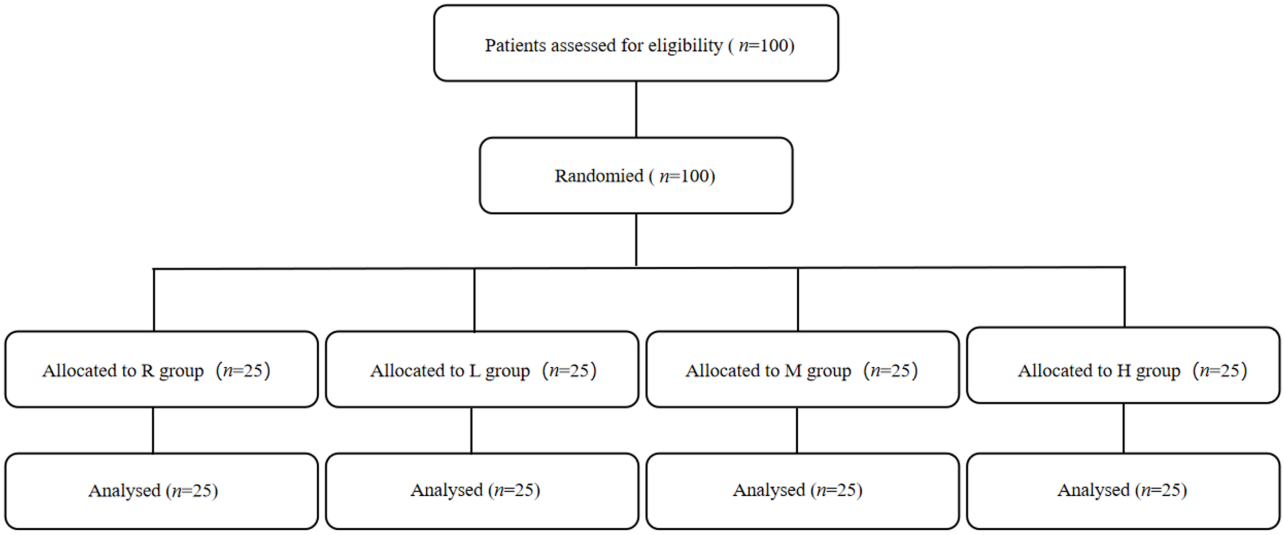

Fig. 2. Flow diagram of subject inclusion and grouping.

Table 1. General characteristics of the four groups.

Variables	R group (n = 25)	L group (n = 25)	M group (n = 25)	H group (n = 25)	$F/\chi^2/H$-value	p
Sex, female, n (%)	5 (20)	2 (8)	4 (16)	6 (24)	2.481	0.479
Age (years)	29.20 ± 7.49	27.92 ± 4.81	29.4 ± 7.96	27.68 ± 5.09	0.454	0.715
BMI (kg/m^2)	24.62 ± 2.25	23.58 ± 1.94	23.47 ± 1.59	23.60 ± 2.07	1.840	0.145
ASA grade I, n (%)	18 (72)	17 (68)	20 (80)	17 (68)	1.190	0.755
Preoperative pain score	2 (1.5, 3)	2 (0, 4)	2 (0.5, 3)	2 (1, 3)	0.635	0.888
Duration of surgery (min)	60 (43, 108)	74 (43, 97.5)	60 (46.5, 83.5)	51 (41.5, 78.5)	0.641	0.887

BMI, body mass index; ASA, American Society of Anesthesiologists.

respectively, maintaining a consistent total volume across groups. Both patients and outcome assessors were blinded to the group allocation to ensure unbiased results; the anesthesiologist preparing the drug solutions was not involved in subsequent data collection or patient assessment. After administration, patients were closely monitored for signs of local anesthetic systemic toxicity and esketamine-related side effects, with vital signs continuously observed and resuscitation equipment readily available in case of emergency. The timing of the ACB was crucial—it was performed after cessation of sevoflurane inhalation and adjustment of propofol along with remifentanil infusion rates to minimize interference with the assessment of sedation levels and to ensure patient safety during emergence from anesthesia. By adhering to these precautions and focusing on key procedural aspects, we aimed to maximize the efficacy of the analgesia plan while minimizing potential risks to the patients.

Outcome and Data Measurement

The primary outcome was the duration of sensory blockade in ACB. To determine this, sensory function was evaluated at regular intervals postoperatively using a standardized pinprick test. A 22-gauge blunt needle was gently applied to the skin along the distribution of the saphenous nerve on the medial aspect of the lower leg. Assessments began once the patients regained full consciousness and were repeated every 30 minutes until they reported normal sensations. Patients were instructed to report whether they felt the pinprick sensation as sharp (normal sensation) or dull (sensory blockade). The duration of sensory blockade was defined as the time elapsed from the completion of the ACB to the first report of normal sharp sensation.

The secondary outcomes included Numerical Rating Scale (NRS) pain scores [22] at rest or during movement immediately after surgery, and at 4, 8, 24, and 48 hours postoperatively. The NRS ranges from 0 (no pain) to 10 (worst imaginable pain), representing a simple numerical rating of pain intensity. The number of postoperative analgesia rescue cases was recorded.

The level of sedation was assessed using the modified observer's assessment of alertness/sedation (MOAA/S) scores [23] within 8 hours postoperatively. The MOAA/S scores range from 0 to 6: 6 = being anxious/agitated; 5 = responding readily to name; 4 = lethargic response to name; 3 = responding only after name is called loudly and/or repeatedly; 2 = responding only after mild prodding or shaking; 1 = responding only after painful trapezius squeeze; 0 = not responding to painful stimulus.

The Quality of Recovery-15 (QoR-15) scores [24] on the first postoperative day were assessed to evaluate postoperative recovery quality. The QoR-15 includes items assess-

ing physical comfort, physical independence, psychological support, emotional state and pain, with each item scored on a scale of 0–10, yielding a maximum score of 150 points where higher scores indicate better recovery quality. Any adverse events occurring within 48 hours postoperatively were documented.

Statistical Analysis

Statistical analysis was performed using SPSS 26.0 (IBM Corporation, Armonk, NY, USA) software. The Shapiro-Wilk test was used to assess the normality of data distribution. For normally distributed continuous data ($p > 0.05$ in the Shapiro-Wilk test), one-way analysis of variance (ANOVA) followed by Tukey's HSD Test was used for comparison between groups and they are presented as mean ± standard deviation ($\bar{x} \pm$ SD). Expressed as median and percentiles, non-normally distributed continuous data ($p < 0.05$ in the Shapiro-Wilk test) were analyzed with Kruskal-Wallis test. If a significant difference was detected ($p < 0.05$), post hoc pairwise comparisons were conducted using Dunn's test with Bonferroni adjustment for multiple testing. Chi-square and Fisher's exact tests were employed for the analysis of categorical data, which are presented as frequencies or percentages in this paper. Two-tailed tests were used in this study, and a $p < 0.05$ was considered statistically significant.

Results

Demographic Characteristics, Preoperative Examination Results, and Perioperative Management

This study ultimately included 100 patients who underwent arthroscopic knee surgery from October 2022 to March 2023, and they were randomly and evenly divided into four groups (Fig. 2). There were no statistically significant differences in sex, age, BMI, ASA classification, preoperative pain scores, or duration of surgery among the four groups of patients ($p > 0.05$) (Table 1).

Baseline and Intraoperative Characteristics

There were no statistically significant differences among the four groups regarding preoperative HR, BP, SpO_2, intraoperative blood loss, or the total doses of anesthetic agents used, including fentanyl, remifentanil, propofol, and sevoflurane ($p > 0.05$). The usage rates of additional medications such as atropine and urapidil were also similar across groups ($p > 0.05$) (Table 2).

Sensory Block and Relief of Postoperative Pain

The duration of sensory block differed significantly among the four groups (Kruskal-Wallis H = 9.87, $p = 0.022$, Table 3, Fig. 3). Post-hoc Dunn's test revealed longer block duration in H group (median [IQR]: 695.56 [648.24–742.88] min) compared to R group (635.64 [604.89–666.39] min, $p = 0.003$) and L group (655.80 [624.92–686.68] min, $p = 0.049$). M group (674.16 [639.90–708.42] min) also showed a longer duration than R group ($p = 0.042$). Postoperative pain assessment revealed significant differences at multiple time points (Table 4). Immediately after surgery, M and H groups demonstrated lower resting NRS scores (median [IQR]: 1 [0–1.5] vs 2 [1–2], $p = 0.008$ and $p = 0.015$ respectively) compared to R group. Similarly, movement NRS scores were lower in M and H groups (1 [1–2] and 2 [1–2] vs 2 [2–3], $p = 0.017$ and $p = 0.011$ respectively). At 8 hours post-surgery, all treatment groups (L, M, and H) achieved significantly lower resting pain scores compared to R group ($p = 0.003$, 0.027, and 0.019, respectively). Movement scores followed a similar pattern ($p = 0.032$, 0.040, and 0.042, respectively).

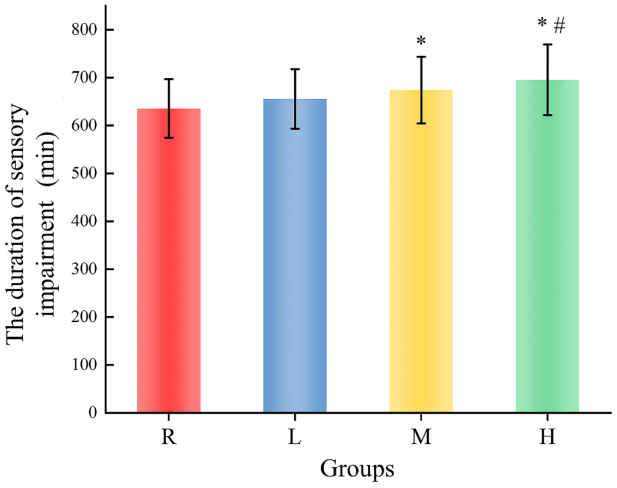

Fig. 3. The comparison of the duration of sensory impairment among the four groups. *$p < 0.05$ compared with R group; #$p < 0.05$ compared with L group.

Sedation Level and Postoperative Recovery Quality

MOAA/S scores showed significant differences immediately post-surgery (H = 16.45, $p = 0.001$), with H group demonstrating lower scores compared to R and L groups ($p = 0.039$ and $p = 0.041$ respectively, Table 5). QoR-15 scores revealed significant differences (F = 12.402, $p < 0.001$), with H group showing lower scores compared to all other groups ($p < 0.001$, $p = 0.001$, and $p = 0.030$ vs R, L, and M groups, respectively, Fig. 4).

Postoperative Adverse Reactions

As shown in Table 6, the incidence of dizziness differed significantly among groups ($\chi^2 = 14.522$, $p = 0.002$), with H group showing higher rates (56%) compared to R (8%, $p < 0.001$), L (24%, $p = 0.021$), and M (28%, $p = 0.045$) groups. Rebound pain showed significant differences ($\chi^2 = 7.937$, $p = 0.047$), with M group demonstrating lower incidence (12%) compared to other groups (R: 44%, $p = 0.012$; L: 36%, $p = 0.047$).

Table 2. Baseline and intraoperative variables of the four groups.

Variables	R group (n = 25)	L group (n = 25)	M group (n = 25)	H group (n = 25)	F/χ^2/H	*p*
Preoperative HR (beats/min)	72.4 ± 6.5	73.1 ± 7.0	71.8 ± 6.8	72.6 ± 7.2	0.153	0.928
Preoperative BP (mmHg)	122.5 ± 9.8	121.8 ± 10.2	123.2 ± 9.5	122.0 ± 10.1	0.099	0.961
Preoperative SpO_2 (%)	98.6 ± 0.8	98.4 ± 0.9	98.5 ± 0.7	98.7 ± 0.6	0.725	0.540
Intraoperative blood loss (mL)	50.2 ± 15.3	48.5 ± 14.8	49.8 ± 16.0	51.0 ± 15.7	0.114	0.952
Fentanyl dose (μg)	22.22 ± 3.56	22.40 ± 2.80	21.52 ± 1.86	22.20 ± 3.20	0.439	0.726
Remifentanil dose (mg)	900 (574, 1612)	900 (600, 1376.25)	884 (685, 1174)	784 (534, 1090)	0.761	0.859
Propofol dose (mg)	225 (148.5, 403)	225 (150, 344)	221 (171.25, 293.5)	196 (133.5, 272.5)	0.772	0.856
Sevoflurane dose (MAC-hours)	13.5 (10, 24.5)	13.5 (10, 20.75)	13.5 (10.5, 18.75)	11.5 (9.5, 17.75)	0.742	0.863
Atropine usage, n (%)	2 (8%)	1 (4%)	2 (8%)	3 (12%)	1.087	0.780
Urapidil usage, n (%)	3 (12%)	2 (8%)	3 (12%)	2 (8%)	0.444	0.931

HR, heart rate; BP, blood pressure; SpO_2, pulse oxygen saturation; MAC, minimum alveolar concentration.

Table 3. Duration of sensory blockade, rescue analgesia, and recovery quality scores of the four groups.

Variables	R group (n = 25)	L group (n = 25)	M group (n = 25)	H group (n = 25)	Test statistic	*p*
Duration of blockade, min†	635.64 (604.89–666.39)	655.80 (624.92–686.68)	674.16 (639.90–708.42)*	695.56 (648.24–742.88)*#	H = 9.87	0.022
Rescue analgesia, *n* (%)	10 (40)	9 (36)	5 (20)	4 (16)	χ^2 = 5.159	0.161

†Data presented as median (IQR); * $p < 0.05$ compared with R group; # $p < 0.05$ compared with L group.

Table 4. Postoperative resting and movement NRS pain scores of the four groups.

Time point	R group (n = 25)	L group (n = 25)	M group (n = 25)	H group (n = 25)	H statistic	*p* value
Resting NRS score						
Immediate	2 (1, 2)	1 (0.5, 1.5)	1 (0, 1.5)*	1 (0, 1.5)*	12.46	0.006
4 h	2 (1, 2)	1 (0, 2)	2 (0.5, 2)	2 (0, 2)	5.82	0.121
8 h	2 (2, 2.5)	1 (0, 2)*	2 (0.5, 2)*	2 (1, 2)*	11.94	0.008
24 h	2 (2, 2)	2 (1, 2)	2 (1, 2)	2 (1, 2)	3.15	0.369
48 h	1 (0, 1)	1 (0, 2)	1 (0, 2)	1 (1, 2)	2.89	0.409
Motion NRS score						
Immediate	2 (2, 3)	2 (1, 3)	1 (1, 2)*	2 (1, 2)*	13.77	0.003
4 h	3 (2, 3)	3 (2, 3)	3 (2, 3)	2 (2, 3)	4.01	0.260
8 h	3 (2, 4)	3 (2, 3)*	2 (2, 3)*	2 (2, 3)*	12.357	0.006
24 h	3 (2, 4)	3 (2, 3.5)	2 (2, 3)	3 (2, 4)	6.89	0.075
48 h	2 (1, 3)	2 (2, 3)	2 (1, 2.5)	2 (0, 3)	2.125	0.547

Data presented as median (IQR); NRS, Numerical Rating Scale; * $p < 0.05$ compared with R group.

Table 5. MOAA/S scores of the four groups.

Time	R group (n = 25)	L group (n = 25)	M group (n = 25)	H group (n = 25)	H statistic	*p*
Immediate	5 (5, 5)	5 (5, 5)	5 (4, 5)	4 (4, 5)*#	16.45	0.001
4 h	5 (5, 5)	5 (5, 5)	5 (5, 5)	5 (5, 5)	3.27	0.353
8 h	5 (5, 5)	5 (5, 5)	5 (5, 5)	5 (5, 5)	0.00	1.000

Data presented as median (IQR); MOAA/S, modified observer's assessment of alertness/sedation; * $p < 0.05$ compared with R group; # $p < 0.05$ compared with L group.

Discussion

Effective pain management is crucial for a speedy recovery following arthroscopic knee surgery. The utilization of femoral nerve block in knee arthroscopy has become a common practice to alleviate postoperative pain. Nonetheless, recent studies have indicated that ACB is equally effective in reliving pain and has the additional benefit of reducing postoperative pain levels and the requirement for opioid medication following procedures like anterior cruciate ligament reconstruction and meniscectomy [25,26]. Moreover, it can contribute to the prompt resumption of daily activities for patients and also reduce the risks of falls [27]. These attributes make ACB a potential optimal analgesic approach for postoperative pain management in arthroscopic knee surgery.

The history of adding adjuvants to local anesthetic solutions for peripheral nerve blocks is long-standing. Ketamine, for example, can antagonize NMDA receptors, inhibit the

Table 6. Adverse reactions experienced by subjects in the four groups.

Event	R group (n = 25)	L group (n = 25)	M group (n = 25)	H group (n = 25)	χ^2	p
Dizziness	2 (8)	6 (24)	7 (28)	14 (56)*#§	14.522	0.002
PONV	6 (24)	7 (28)	10 (40)	12 (48)	4.000	0.261
Leg weakness	1 (4)	2 (8)	2 (8)	1 (4)	0.722	0.868
Rebound pain	11 (44)	9 (36)	3 (12)*#	5 (20)	7.937	0.047
Sleep disorders	7 (28)	6 (24)	1 (4)	3 (12)	6.449	0.092
Hallucinations	0 (0)	0 (0)	0 (0)	1 (4)	3.030	0.387

Data presented as n (%); PONV, postoperative nausea and vomiting; *$p < 0.05$ compared with R group; #$p < 0.05$ compared with L group; §$p < 0.05$ compared with M group.

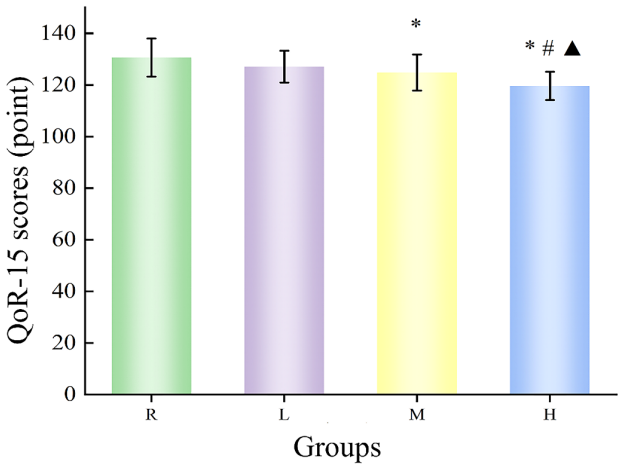

Fig. 4. The comparison of QoR-15 scores among the four groups. *$p < 0.05$ compared with R group; #$p < 0.05$ compared with L group; ▲$p < 0.05$ compared with M group. QoR-15, Quality of Recovery-15.

conduction of nociceptive stimuli, suppress peripheral inflammation, and provide some neuroprotective effects. Ketamine can also impede sodium ion channels and exhibit local anesthetic properties, leading to an increased excitatory threshold and decreased nerve conduction velocity [28]. When ketamine is used in combination with local anesthetics, it can enhance the blocking effect of local anesthetics, reduce central sensitization and breakthrough pain caused by NMDA receptors, and potentially prevent the incidence of chronic pain [29]. However, the utilization of ketamine is restricted due to its propensity to cause specific psychomotor reactions, such as the emergence of delirium and agitation during clinical application [30]. S (+)-ketamine, also known as esketamine, is the right-handed enantiomer of ketamine. It has approximately four times the anesthetic potency of ketamine and significantly reduces dose-dependent side effects [31]. This study investigated the potential advantages of administering esketamine as an adjuvant in ACB during arthroscopic knee surgery under general anesthesia. Adding esketamine results in low plasma concentration and side effect reduction, while still producing local effects. The impact of esketamine on block duration, postoperative analgesia, recovery quality, and adverse reactions were evaluated. Postoperative pain was managed with non-steroidal anti-inflammatory drugs administered either orally or intramuscularly. The results of this study could shed light on using esketamine as an adjuvant in regional anesthesia.

This study found that adding 30 or 40 mg of esketamine can prolong nerve block duration and decrease post-surgery pain scores for patients at rest and during motion, potentially due to systemic effects on the bloodstream. The adductor canal, located between the sartorius muscle, the medial quadriceps muscle, and the adductor magnus muscle, can be targeted by esketamine injection at subanesthetic doses. This produces analgesic effects by absorption into the bloodstream through the capillaries in the muscle tissue via osmosis. The reduction in MOAA/S scores right after surgery in the subjects taking 30 and 40 mg esketamine reinforces this hypothesis. At the 8-hour mark after surgery, pain scores across all three esketamine groups exhibited lower levels compared to the control group. This suggests that the incorporation of an appropriate dose of esketamine to the nerve block with ropivacaine can augment early postoperative pain relief. This may be due to the analgesic properties of esketamine itself and local anesthetic characteristics.

The concentration range of esketamine employed in this study was approximately 0.27 mg/kg to 0.54 mg/kg, which aligns with the subanesthetic dose range frequently used in clinical practice. Previous studies have shown that intravenous administration of subanesthetic doses of esketamine can produce adequate analgesia without inducing dissociative anesthesia [32,33]. Throughout this study, no hallucinations or similar reactions were noted. Nevertheless, patients administered a high dose of esketamine exhibited a significant reduction in their immediate postoperative MOAA/S scores and recovery quality on the first day following surgery. Additionally, the frequency of postoperative dizziness increased with elevated doses of esketamine. Previous research has indicated that esketamine may reduce central sensitization and decrease rebound pain after nerve blockade [34]; this study identified a declining trend in rebound pain after nerve blockade with the addition of esketamine. The addition of 30 mg of esketamine led to a notable reduction in rebound pain after a nerve blockade. However, due to the limited sample size in this study, further observation is necessary to validate this effect.

Several limitations of this study merit acknowledgment. Firstly, the follow-up period was confined to 48 hours post-operation, thereby precluding an exploration of esketamine's potential influence on long-term chronic pain. Secondly, the study encompassed a modest sample size, underscoring the necessity for broader clinical trials across multiple centers to comprehensively scrutinize the effectiveness of esketamine as an adjuvant.

Conclusions

In contrast to using ropivacaine alone for ACB, incorporating esketamine as an adjuvant demonstrates the potential to prolong the duration of the sensory blockade and enhance early postoperative pain relief. It is advisable to consider a dosage range of 20 to 30 mg, as higher doses of esketamine could potentially harm post-anesthesia recovery.

Availability of Data and Materials

The data used to support the findings of this study are available from the corresponding authors upon request.

Author Contributions

SLZ, ZQL, HJC and YJS and YGD conceptualized the research study and designed the experiments. SLZ, ZQL, SQZ, JHW and XYM performed the data collection and conducted the experiments. SLZ and ZQL analyzed and interpreted the data. SLZ, ZQL and SQZ wrote the initial draft of the manuscript. HJC and YJS provided critical revisions to the manuscript. All authors contributed to important editorial changes in the manuscript. All authors read and approved the final manuscript. All authors have participated sufficiently in the work and agreed to be accountable for all aspects of the work.

Ethics Approval and Consent to Participate

This study was approved by the Medical Ethical Committee of the General Hospital of Northern Theater Command Y(2022)093. The drugs under investigation were administered only after obtaining informed consent from the patients or their family members. The trial was conducted in adherence to the principles of the Declaration of Helsinki and reported following the Consolidated Standards of Reporting Trials (CONSORT) 2013 guidelines.

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Conflict of Interest

The authors declare no conflict of interest.

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