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The efficacy and safety of patient-controlled intravenous analgesia with esketamine after total hip arthroplasty: a randomized controlled trial

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Abstract

Purpose To evaluate the efficacy and safety of esketamine-based patient-controlled intravenous analgesia following total hip arthroplasty.

Methods A total of 135 total hip arthroplasty patients were randomly assigned to one of the three treatment groups: esketamine, sufentanil or continuous fascia iliaca compartment block (FICB) group. The primary endpoint was the postoperative visual analogue scale (VAS) pain scores at rest and on movement. Secondary endpoints included preoperative 1-day and postoperative 7-day Self-Rating Anxiety Scale (SAS) and Self-Rating Depression Scale (SDS) scores, the satisfaction of patients and surgeons, postoperative 1-month and 3-month Harris function scores, the incidence of adverse reactions.

Results At 48 h post-surgery, the VAS pain scores in the esketamine and FICB groups at rest and on movement were significantly lower than those in the sufentanil group ($P<0.05$). The satisfaction of patients in the esketamine group was higher than that in the sufentanil and FICB groups ($P=0.014$). The satisfaction of surgeons in the esketamine and FICB groups was higher than that in the sufentanil group ($P=0.002$). At postoperative day 7, the SAS scores and SDS scores in the esketamine group were significantly lower than those in the sufentanil and FICB groups ($P<0.05$). Compared with the sufentanil group, the postoperative nausea and vomiting, dizziness and total adverse reactions in the esketamine group and FICB group were lower ($P<0.05$).

Conclusion Patient-controlled intravenous analgesia with esketamine has the potential to provide good postoperative analgesia for total hip arthroplasty patients, reduce the incidence of adverse reactions after the operation, improve the satisfaction of patients and surgeons, and significantly improve patients' postoperative mood.

Trial registration : ChiCTR2300069632 (https://www.chictr.org.cn/) (March 22th, 2023).

Keywords Total hip arthroplasty, Esketamine, Fascia Iliaca compartment block, Patient controlled intravenous analgesia, Postoperative pain

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Introduction

In orthopedics, total hip arthroplasty (THA) is a common procedure. By 2030, there will likely be 3.5 million THA surgeries performed annually, which is a public health concern [1]. Studies have found that 35–80% of patients experience moderate to severe pain 1–5 days after THA, and 26–58% of patients still report hip pain six months after surgery [2, 3]. Severe postoperative pain can hinder early joint mobility and rehabilitation, disrupt sleep, lead to cognitive dysfunction, increase anxiety and reduce patient satisfaction, and increase the risk of thromboembolic disorders and infections [4, 5]. If acute pain is not managed promptly, it can result in long-term psychological and emotional suffering, which can eventually turn into more difficult-to-control chronic pain [3]. Therefore, pain after THA is a major concern for clinicians and patients, and effective postoperative pain management is essential to improve patient satisfaction and clinical prognosis.

At present, the main methods used to manage pain after THA include local infiltration analgesia, epidural analgesia, patient-controlled intravenous analgesia (PCIA) and peripheral nerve block. The application of peripheral nerve block in postoperative analgesia is becoming increasingly common, among which fascia iliaca compartment block (FICB) is one of the most commonly used methods. FICB is a type of fascial space block in which local anesthetics reduce hip pain by blocking the lateral femoral cutaneous nerve, femoral nerve, and obturator nerve [6]. FICB with ultrasound guidance has become a reliable analgesic option for THA in recent years. However, studies have shown that it affects the perception of touch and temperature in the operated limb, reduces the muscle strength of the quadriceps, hinders postoperative mobilization, increases hospitalization expenses, and reduces patient satisfaction [7–9]. Therefore, the analgesic method of peripheral nerve block still needs to be further optimized. Opioid analgesia remains the mainstay of acute postoperative pain management for THA because of its powerful analgesic effect [10]. In a meta-analysis of 570 clinical trials, up to 54% of trials reported opioid use after THA, with up to 21 mg of morphine equivalent consumed within 24 h [11]. However, the use of opioids often leads to many adverse reactions, such as respiratory depression, excessive sedation, nausea and vomiting, itching, and drug addiction [9, 10, 12]. These adverse reactions reduce the satisfaction of surgeons and patients, increase patient hospitalization costs, and hinder the early recovery of patients after operation. Therefore, finding an effective analgesic method with fewer side effects is critical.

Esketamine is an N-methyl-D-aspartate (NMDA) receptor blocker and a dextroisomer of ketamine, which has a higher anesthetic titer and fewer adverse reactions, and has been used for anesthesia, analgesia, sedation, and anti-depression [13, 14]. Studies have shown that in elective cesarean delivery and gynecological laparoscopy surgery, intraoperative esketamine infusions can effectively reduce postoperative pain, reduce opioid consumption during the perioperative period, and reduce the incidence of adverse events after surgery [15, 16]. All of the above studies showed that esketamine used in perioperative patients can effectively reduce postoperative pain and does not increase the incidence of postoperative adverse reactions, which has good clinical application value. However, there are few reports on PCIA with esketamine after THA. It is still unclear whether esketamine can provide a good analgesic effect and reduce postoperative adverse reactions in THA, and its efficacy and safety need to be further explored. The objective of our study was to investigate the efficacy and safety of esketamine for PCIA following THA, and to provide a new treatment method and theoretical basis for reducing postoperative analgesia-related adverse reactions after THA.

Methods

Study design and settings

This was a single-center, randomized controlled clinical trial. Our study was approved by The Ethics Committee (registration number :2022 – 423). This study protocol was registered at the Chinese Clinical Trial Registry (https://www.chictr.org.cn/, identifier: ChiCTR2300069632) on March 22th, 2023. All patients signed informed consent before operation.

A total of 135 patients with elective THA surgery were enrolled in our study, who were aged 18–85 years and had American Society of Anesthesiologists (ASA) physical status I-III. Exclusion criteria included mental illness or cognitive impairment, allergic to or contraindicated for the study drug, had diabetes, peripheral or central neuropathy, liver or kidney failure, severe cardiovascular or respiratory disease, or inability to understand or communicate. An independent nurse assessed depression and anxiety on the day before the operation using the Self-Rating Depression Scale (SDS) and the Self-Rating Anxiety Scale (SAS).

Eligible participants were randomized at a 1:1:1 ratio to the esketamine group, the sufentanil group, or the FICB group using a computer-generated random table (http://www.randomization.com). Because our analgesia met hods were different, double-blinding was not possible. Patient postoperative data were collected by an independent nurse who was not involved in the study.

Surgical procedures

The THA surgery was performed using a standard posterolateral approach. Patients were positioned in a 90° lateral decubitus position with the affected side facing

upward. A curved incision approximately 10 cm in length was made from below the posterior superior iliac spine to the posterior side of the greater trochanter of the femur. The incision was carried out layer by layer through the skin, subcutaneous tissue, and lateral femoral myofascia. The hip joint was adducted and internally rotated to expose the piriformis muscle. The piriformis muscle was severed at its attachment point to the greater trochanter, exposing the joint capsule. A T-shaped incision was made in the joint capsule to expose the femoral head and neck. The femoral neck was osteotomized 1–1.5 cm above the lesser trochanter, and the femoral head was extracted and measured for its diameter. The acetabulum was then exposed and cleaned, and its round ligament was resected along with the acetabular labrum. Using an acetabular rasp, the acetabulum was gradually enlarged and reamed at an abduction of 45° and anteversion of 15°, ensuring complete removal of acetabular cartilage down to the subchondral bone. After rinsing the acetabulum, the acetabular prosthesis was implanted at the same angles (45° abduction and 15° anteversion) and an appropriate liner was placed. Subsequently, an opener was used to open the femoral end and a medullary cavity file was inserted with a 15° anteversion to sequentially ream to the cortical bone. An appropriately sized prosthetic stem was implanted, followed by the placement of the trial component and the restoration of the hip joint. Following the mobility assessment of the hip joint in all directions, if no dislocation was observed and the tightness was appropriate, the corresponding femoral head prosthesis was selected for implantation. After thorough irrigation, a drainage tube was placed, and finally the incision was closed layer by layer. All procedures were performed by Dr. Wenyuan Luo and his team from the Department of Orthopedics at Gansu Provincial Hospital.

Analgesia and postoperative analgesia management

Heart rate, peripheral pulse oximeter value, blood pressure, and electrocardiogram were routinely monitored after patients entered the room. All patients were given intravenous injections of 0.05 mg/kg midazolam, 0.6 mg/kg sufentanil, 2 mg/kg propofol, and 0.6 mg/kg rocuronium for analgesia induction, and muscle relaxation was followed by tracheal intubation and mechanical ventilation. Target-controlled infusions (TCIs) of propofol (2–4 ug/ml) and remifentanil (3–5 ng/ml), as well as inhalation of 2–3% sevoflurane, were used to maintain anesthesia. Injections of 5 mg cisatracurium were given intermittently as needed to maintain neuromuscular blockade. Throughout the procedure, the bispectral index (BIS) value was kept between 40 and 60, and fluctuations in heart rate and blood pressure were restricted to 20% of the preoperative baseline values. All patients were operated on by the same team.

After the operation, according to our study design, the analgesics used in the esketamine group were 1.5 $mg{\cdot}kg^{-1}$ esketamine + 250 mg flurbiprofen axetil + 0.9% normal saline to 150 ml. The analgesics used in the sufentanil group were 2.0 $\mu g{\cdot}kg^{-1}$ sufentanil + 250 mg flurbiprofen axetil + 0.9% normal saline to 150 ml. The analgesic pump parameters were as follows: the first dose was 4 ml; continuous infusion volume was $3ml{\cdot}h^{-1}$; bolus dose was 2 ml; patient lockout time was 15 min. In the FICB group, the FICB was operated by the same anesthesiologist with extensive experience in nerve blocks with a "bow tie sign". Under ultrasound guidance, 20 ml of 0.2% ropivacaine was injected to ensure adequate fluid diffusion and expand the plane, and then a catheter was inserted around 5 cm deep through the sheath tube. To keep the catheter from dislodging, a 3-cm subcutaneous tunnel was created. The FICB group received 300 ml of 0.2% ropivacaine, with the pump parameters of the first dose 20 ml, 20 ml/4 h pulse pumping, a bolus dose of 5 ml, and a lockout time of 30 min. As a rescue strategy, tramadol 100 mg was injected if the postoperative Visual Analog Scale (VAS) pain score at rest remained greater than 3 after two bolus injections.

Study outcomes

The primary endpoint of our study was the pain scores at rest and on movement (passive leg lift 30 degrees) as assessed by the VAS at different times after surgery (where 0 indicated no pain and 10 indicated maximal pain).

The secondary endpoints included preoperative 1-day and postoperative 7-day SAS scores (normal mental state is 0–49, mild anxiety is 50–59, moderate anxiety is 60–69, and severe anxiety is over 69) and SDS scores (normal mental state is 0–53, mild depression is 53–62, moderate depression is 63–72, and severe depression is greater than 72), Harris functional scores of the hip joint at postoperative 1 month and 3 months, time to first walk, hospital stay (from the first day after surgery to discharge), the satisfaction of patients and surgeons (0–10, 0 = unsatisfied and 10 = very satisfied), the number of patients with remedial analgesia, tramadol consumption, time to first remedial analgesia, and bromage motor block scores. The tactile and temperature sensation of the limb were assessed using a three-level scale (0 = nonexistence, 1 = decline, and 2 = intact), an alcohol swab was used to measure patients' temperature sensation, and the blunt end of a cotton swab was used to measure their touch sensation. The incidence of adverse reactions such as postoperative nausea and vomiting (PONV), dizziness, sedation, and nightmare.

During the whole trial, the adverse reactions of all patients and the toxicity of the local anesthetics were closely monitored.

Sample size calculation

Sample sizes were calculated by repeated measures analysis using PASS version 2021 software. According to a pilot study with 12 patients in each group, the mean VAS scores at rest in the three groups at different time points were 1.90, 2.27, 2.83, and 1.39 for the FICB group; 2.31, 2.64, 2.23, and 1.62 for the esketamine group; and 0.8, 1.5, 0.8, and 1.2 for the sufentanil group. Assuming an alpha of 0.05 and a power of 0.9, each group in this trial needed 45 patients, assuming a 5% dropout rate.

Statistical analysis

Statistical data analysis was conducted using SPSS statistical software (version 26.0). Shapiro-Wilk tests were performed to determine if data were normally distributed. Normally distributed data are displayed as means (standard deviations, SDs), and analyzed by one-way analysis of variance (ANOVA). Significant group differences were further analyzed using Tukey's post hoc test. Non-normally distributed data were shown as median (interquartile range) and analyzed by Kruskal-Wallis test. The qualitative data were analyzed using χ^2 tests and are presented as percentages or numbers. *P* less than 0.05 was the significance level.

Results

Our study included a total of 135 patients who were randomly assigned to three groups: sufentanil group (45 patients), FICB group (45 patients), and esketamine group (45 patients). One patientin the esketamine group was lost to follow-up due to a telephone malfunction, and one catheter occlusion in the FICB group was excluded from the analysis. Ultimately, 133 patients completed the study (Fig. 1). The baseline demographic and clinical characteristics of the patients, such as gender composition, age, body mass index (BMI), ASA classification, operation time, and surgical bleeding volume, were comparable among the three groups with no significant differences ($P > 0.05$) (Table 1).

At 48 h postoperatively, the esketamine and FICB groups had significantly lower VAS pain levels at rest and on movement than the sufentanil group ($P < 0.05$). The three groups did not differ significantly at other time points (Fig. 2).

At all time points, patients' temperature and tactile sensation scores in the esketamine and sufentanil groups were significantly higher than those in the FICB group ($P < 0.001$) (Table 2). No significant differences in the bromage scores were found among the three groups at all time points ($P > 0.05$) (Table 3).

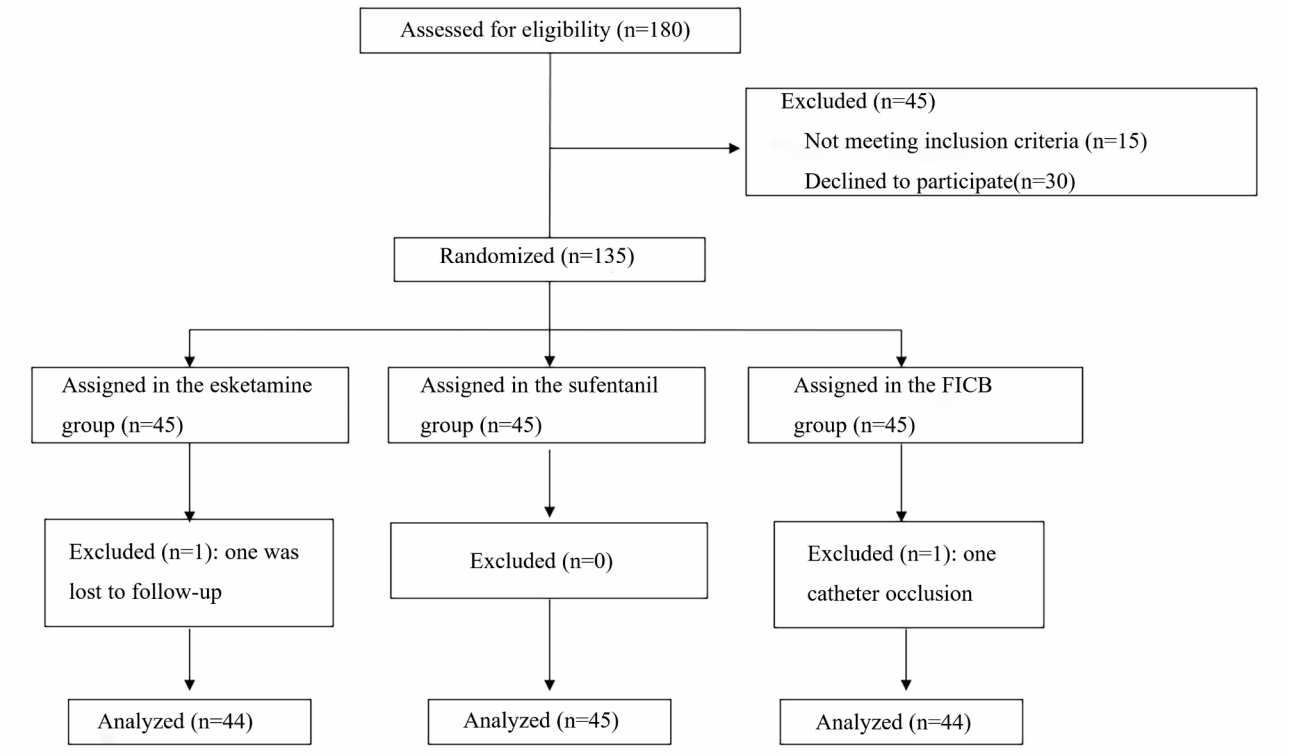

Fig. 1 Flow chart of this study. 135 patients were enrolled in this study. One patient from the esketamine group was lost to follow-up due to the phone not connected, one catheter occlusion in the FICB group was eliminate. Therefore, 133 patients had completed the study

Table 1 Baseline demographic and clinical characteristics

Variables	Sufentanil group (*n* = 45)	FICB group (*n* = 44)	Esketamine group (*n* = 44)	*P* value
Age (yr), mean (SD)	61.3 (15.0)	58.7 (15.7)	59.3 (14.6)	0.691
Female, n/total N (%)	22/45 (49%)	20/44 (45%)	25/44 (57%)	0.550
BMI ($kg.m^{-2}$), mean (SD)	23.7(3.5)	23.5(3.3)	22.9(3.1)	0.468
ASA, n/total N (%)				0.355
I	4/45 (9%)	8/44 (18%)	10/44 (23%)	
II	32/45 (71%)	31/44 (71%)	26/44 (59%)	
III	9/45 (20%)	5/44 (11%)	8/44 (18%)	
Operation time (min), mean (SD)	114 (32)	104 (20)	105 (29)	0.209
Blood loss (ml), median (IQR)	300 (200–400)	200 (100–375)	300 (200–400)	0.289

Notes: Data are expressed as mean (SD), median (IQR), or n/total N (%). ASA = American Society of Anesthesiologists; BMI = body mass index; IQR = interquartile range; SD = standard deviation

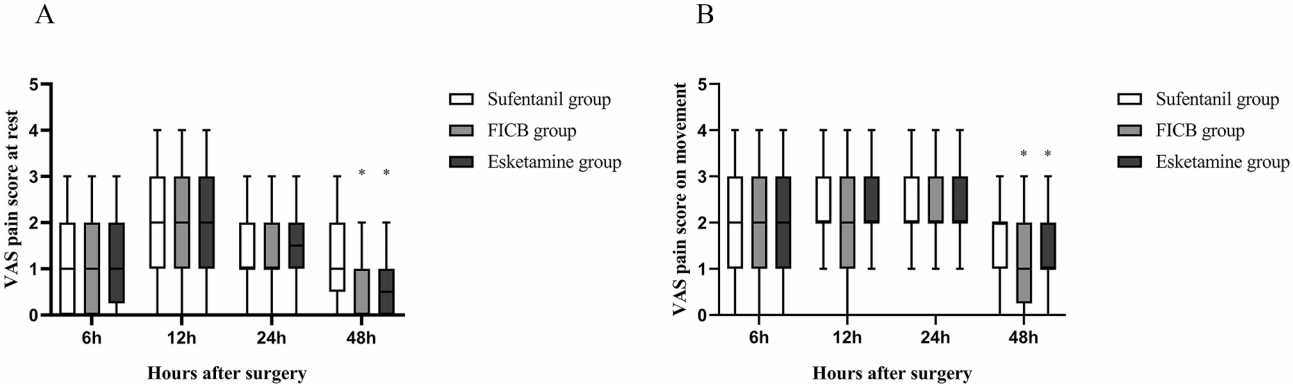

Fig. 2 Comparison of postoperative VAS pain scores at rest (**A**) and on movement (**B**) among the three groups. $^{*}P < 0.05$, compared with the sufentanil group

Table 2 Patient's temperature and tactile scores compared among the three groups

Variables	Time interval	Sufentanil group (*n* = 45)	FICB group (*n* = 44)	Esketamine group (*n* = 44)	Kruskal-Wallis	*P* value
Temperature sensation score	6 h	2 (2, 2) $^{\#}$	0 (0, 1)	2 (2, 2) $^{\#}$	87.508	<0.001
	12 h	2 (2, 2) $^{\#}$	0 (0, 1)	2 (2, 2) $^{\#}$	101.166	<0.001
	24 h	2 (2, 2) $^{\#}$	0 (0, 0)	2 (2, 2) $^{\#}$	106.060	<0.001
	48 h	2 (2, 2) $^{\#}$	0 (0, 1)	2 (2, 2) $^{\#}$	88.176	<0.001
Tactile score	6 h	2 (2, 2) $^{\#}$	0 (0, 1)	2 (2, 2) $^{\#}$	75.616	<0.001
	12 h	2 (2, 2) $^{\#}$	0 (0, 1)	2 (2, 2) $^{\#}$	94.547	<0.001
	24 h	2 (2, 2) $^{\#}$	0 (0, 1)	2 (2, 2) $^{\#}$	101.518	<0.001
	48 h	2 (2, 2) $^{\#}$	0 (0, 1)	2 (2, 2) $^{\#}$	90.399	<0.001

Notes: Data are presented as median (IQR). $^{\#}P < 0.05$, compared with the FICB group; *P* value from Kruskal-Wallis test. IQR = interquartile range

Table 3 Patient's bromage scores compared among the three groups

Variables	Time interval	Sufentanil group (*n* = 45)	FICB group (*n* = 44)	Esketamine group (*n* = 44)	Kruskal-Wallis	*P* value
Bromage score	6 h	2 (2, 2)	2 (2, 2)	2 (2, 2)	0.625	0.732
	12 h	2 (1, 2)	1 (1, 2)	1 (1, 2)	2.145	0.342
	24 h	1 (1, 1)	1 (1, 1)	1 (1, 1)	0.537	0.765
	48 h	1 (1, 1)	1 (1, 1)	1 (1, 1)	1.867	0.393

Notes: Data are presented as median (IQR). *P* value from Kruskal-Wallis test. IQR = interquartile range

Table 4 Postoperative adverse reactions compared among three groups [n (%)]

Group	PONV	Dizziness	Sedation	Hallucination	Nightmare	Total
Sufentanil group ($n=45$)	16 (35.6%)	11 (24.4%)	2 (4.4%)	0 (0.0%)	0 (0.0%)	23 (51.1%)
FICB group ($n=44$)	7 (15.9%)*	4 (9.1%)*	0 (0.0%)	0 (0.0%)	0 (0.0%)	10 (22.7%)*
Esketamine group ($n=44$)	6 (13.6%)*	3 (6.8%)*	0 (0.0%)	0 (0.0%)	0 (0.0%)	8 (18.2%)*
χ^2/ Fisher	7.609	7.016	2.629	-	-	13.336
P value	0.022	0.03	0.328	>0.999	>0.999	0.001

Notes: Data are expressed as numbers (percentage). Abbreviations: PONV = Postoperative Nausea and Vomiting. *$P<0.05$, compared with the sufentanil group. The qualitative data were analyzed using χ^2 tests

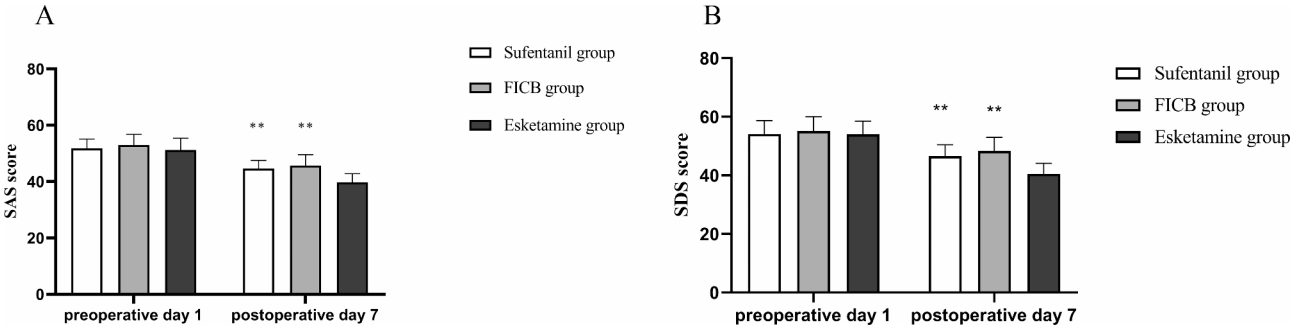

Fig. 3 Self-Rating anxiety Scale (SAS) scores (**A**) and Self-Rating depression Scale (SDS) scores (**B**) were compared among the three groups. **$P<0.05$, compared with the esketamine group

Table 5 Secondary outcomes among the three groups

Variables	Sufentanil group ($n=45$)	FICB group ($n=44$)	Esketamine group ($n=44$)	Test Statistic	*P* value
Time to first walk (h)	40 (3)	38 (4)*	37 (5)*	11.373 (F)	<0.001
Satisfaction of patients	8 (7, 9) **	8 (7, 9) **	9 (8, 9)	8.481 (Kruskal-Wallis)	0.014
Satisfaction of surgeons	8 (7, 9)	9 (8, 9) *	8.5 (8, 9) *	12.644 (Kruskal-Wallis)	0.002
Length of hospital stay(d)	9 (8, 11)	8 (7, 11)	9 (7, 10.75)	2.047 (Kruskal-Wallis)	0.359
Number of patients with remedial analgesia (n, %)	10 (22.2%)	9 (20.5%)	7 (15.9%)	0.598 (χ^2)	0.742
Tramadol consumption (mg)	38 (12)	34 (12)	25 (10)	0.343 (F)	0.710
Time of first remedial analgesia (mine)	150 (55)	106 (33)	90 (33)	1.219 (F)	0.315
Harris score after 1 month	67 (7)	69 (5)	68 (6)	1.051 (F)	0.353
Harris score after 3 months	84 (6)	86 (5)	85 (5)	1.596 (F)	0.207

Notes: Data are expressed as mean (SD), median (IQR), or number (percentage). *$P<0.05$, compared with the sufentanil group. **$P<0.05$, compared with the esketamine group. Continuous data was compared using one-way analysis of variance (ANOVA), median values were compared by Kruskal-Wallis test and the qualitative data were analyzed using χ^2 tests. IQR = interquartile range; SD = standard deviation

Compared with the sufentanil group, the esketamine and FICB groups had significantly lower rates of PONV, dizziness, and total postoperative adverse reactions ($P< 0.05$).There was no statistical difference in sedation, hallucination, and nightmare among the three groups ($P>0.05$) (Table 4).

There were no significant differences in preoperative SAS and SAD scores among the three groups ($P>0.05$). However, at postoperative day 7, the esketamine group showed significantly lower SAS scores and SDS scores compared to the sufentanil and FICB groups ($P<0.05$) (Fig. 3).

In both the esketamine and FICB groups, the satisfaction levels of surgeons were significantly higher compared to the sufentanil group after surgery ($P=0.002$). The satisfaction of patients in the esketamine group was higher than that in the sufentanil and FICB groups ($P=0.014$). Compared with the sufentanil group, the time to first walk in the esketamine and FICB groups were significantly shorter after operation ($P<0.001$). However, there were no significant differences observed among the three groups in terms of the length of hospital stay, number of patients with remedial analgesia, tramadol consumption, time to first remedial analgesia, and Harris score at postoperative 1 month and 3 months ($P>0.05$) (Table 5).

Discussion

Our study found that PCIA with esketamine reduced the VAS pain score of THA patients 48 h after surgery, which was comparable to the analgesic effect of continuous FICB, reduced the incidence of postoperative adverse reactions, promoted the early postoperative activity of patients, and improved the postoperative satisfaction of patients and surgeons. At the same time, the postoperative mood of THA patients was effectively improved. PCIA with Esketamine can provide safe and effective postoperative analgesia for THA patients and provide reference for clinical weak opioid analgesia.

In our study, we observed no significant difference in the postoperative VAS pain scores at 6 h, 12 h and 24 h among the three groups. However, at 48 h postoperatively, patients who received continuous infusion of esketamine and continuous FICB showed significantly lower pain scores compared to those who received sufentanil. Postoperative pain is influenced by various factors such as surgical trauma, central sensitization, and the release of inflammatory mediators [17]. Esketamine, a dextroisomer of ketamine with higher anesthetic and analgesic potency and fewer adverse reactions, exerts its analgesic effects through multiple receptors or pathways. In addition to noncompetitively antagonizing NMDA receptors, esketamine can also produce potent analgesic effects by activating opioid receptors (μ and δ receptors) or increasing norepinephrine and serotonin levels in vivo to activate the descending nociceptive system [18]. By controlling NMDA receptor activation, esketamine has an anti-hyperalgesia effect, reducing hyperalgesia and pain sensitivity caused by opioid drugs [19]. Yu et al. [20, 21] conducted studies which demonstrated that esketamine, compared to opioids, can also reduce the release of postoperative inflammatory factors IL-6 and TNFα, thereby providing analgesic effects. Therefore, our findings suggest that PCIA with esketamine can offer effective postoperative analgesia in patients undergoing THA, with a similar efficacy to continuous FICB. This indicates that esketamine PCIA may be considered as a viable analgesic strategy following THA.

We documented the occurrence of postoperative adverse reactions in the three groups, and the findings indicated that the postoperative PONV, dizziness, and total incidence of adverse reactions in the esketamine PCIA group were significantly lower compared to those in the sufentanil PCIA group. Meng [22] et al. found that after hip replacement in elderly patients, compared with 2.5 μg/kg sufentanil, 2.5 mg /kg esketamine for PICA had a lower incidence of postoperative nausea, vomiting, and dizziness. As a non-opioid drug, esketamine has a lower incidence of postoperative adverse reactions. In addition to digestive adverse reactions, it may also lead to mental adverse reactions such as multiple dreams, nightmares, multilingual, hallucinations, and irritability [23]. The mental adverse reactions of esketamine were dose-dependent, and the risk of hallucinations, nightmares and other psychogenic adverse reactions was not increased by intravenous injection of low dose esketamine [18]. Due to the combination of non-steroidal anti-inflammatory drugs and the use of a lower dose of esketamine (1.5 mg/kg), no adverse mental reactions such as nightmares, hallucinations, and multilingualism were observed in patients. Therefore, in the PCIA with esketamine group, the time to first walk was significantly shortened, and the satisfaction of patients and surgeons was higher. In the continuous FICB group, 7 patients experienced PONV and 4 patients had dizziness, which we think should be related to anaesthesia and surgery. Postoperative PONV and dizziness are common adverse reactions after anesthesia and surgery, with an incidence of about 30% in the general surgical population [24, 25]. Therefore, we think that esketamine intravenous controlled analgesia can provide safe and effective analgesia for THA patients.

Our study found that continuous FICB significantly reduced the tactile and temperature scores of the affected limb. Previous studies have shown that in addition to postoperative pain, postoperative skin numbness can also seriously affect the postoperative satisfaction of patients [26, 27]. Postoperative satisfaction was significantly lower in the continuous FICB group than in the PCIA with esketamine group due to skin numbness in the affected limb. Our study showed that the injection of 0.2% ropivacaine with a 20 ml/4 h pulse pump allowed the local anesthetics to fully diffuse into the fascia cavity and effectively provided analgesia, and did not reduce the muscle strength. This may be related to the pharmacological properties of ropivacaine, showing the separation of motor and sensory blocks. Jun Yao et al. [28] found that using 0.2% ropivacaine for nerve block after lower limb surgery could effectively provide postoperative analgesia while maintaining motor ability and achieving a good separation of sensory and motor block, which aligns with our study. There was no significant difference in postoperative Harris hip function scores among the three groups, we believe that the Harris score of the hip joint after the operation is mainly influenced by surgical factors. Compared with continuous FICB, PCIA with esketamine did not cause skin numbness in the affected limb, and patients were more satisfied.

Compared with continuous FICB and PCIA with sufentanil, the PCIA with esketamine resulted in significantly lower postoperative 7-day SAS and SDS scores, effectively improving the postoperative mood of THA patients. It has been observed that 20–30% of patients experience emotional disorders such as anxiety and depression before surgery due to long-term chronic joint pain and dysfunction [29, 30]. These emotional

disorders are associated with various negative outcomes, including increased medical and surgical complications, postoperative pain and chronic pain, opioid use, perioperative disability, and postoperative dissatisfaction [31–33]. Esketamine, a non-competitive antagonist of the NMDA receptor, exhibits a strong antidepressant effect and improves patients' mood after surgery [34, 35]. The commonly recognized antidepressant mechanism is esketamine-mediated glutamatergic transmission, which results in amino-3-hydroxy-5-methyl-4- isoxazole-propionic acid receptor (AMPAr) activation, increases glutamate release and the synthesis of brain-derived neurotrophic factor (BDNF) [36, 37]. The improvement of patients' mood after surgery can not only improve the satisfaction of patients after surgery, but also accelerate the early recovery. Compared with the PCIA with sufentanil group and continuous FICB group, PCIA with esketamine significantly improved patients' postoperative mood and was more conducive to patients' postoperative recovery.

The main strength and novelty of this study is that it is the first to demonstrate that PICA with esketamine, compared to PICA with sufentanil or continuous FICB, not only provides effective analgesia but also exhibits an opioid-sparing effect, significantly reducing opioid-related adverse effects in postoperative pain management for THA. Additionally, this study is pioneering in its application of a 20 ml/4 h pulsed administration strategy for continuous FICB, demonstrating a good postoperative analgesic effect. Nevertheless, this study still has several limitations. First, the assessment of patient and surgeon satisfaction has no basis in the literature, which may have subjective errors and lack objective indicators. Second, because continuous nerve block and PCIA are different from each other, it can't be double-blind. Further research should be carried out to solve these limitations.

Conclusions

PCIA with esketamine has the potential to provide good postoperative analgesia for THA patients, reduce the incidence of adverse reactions after the operation, improve the satisfaction of patients and surgeons, and significantly improve patients' mood after the operation.

Abbreviations

SD	Standard deviation
IQR	Interquartile range
ASA	American Society of Anesthesiologists
BMI	Body mass index
PONV	Postoperative Nausea and Vomiting
SAS	Self-Rating anxiety Scale
SDS	Self-Rating depression Scale

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Author contributions

WJY conceptualized the study and critically revised the project. WJZ was responsible for data collection and statistical analysis.HJZ, FD and RJL were responsible for the anesthesia and analgesia of the patients.SQ prepared the initial draft of the paper, and he also revised and edited the manuscript.All authors read the final draft of the manuscript and approved it.

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Data availability

the data supporting the findings of this study are available on request from the corresponding author and with permission from the anesthesiology and operation department, Gansu provincial hospital.

Declarations

Ethical approval and consent to Participate

This study was approved by the Research Ethics Committees of Gansu Provincial Hospital (Ethical code: 2022 – 423) and was registered at the Chinese Clinical Trial Registry (https://www.chictr.org.cn/, identifier: ChiCTR2300069632) on March 22th, 2023. Written informed consent was obtained from the patients to publish this article in accordance with the journal's patient consent policy. The study was conducted in accordance with the Declarations of Helsinki, and adhered to the CONSORT guidelines.

Consent for publication

N/A.

Competing interests

The authors declare no competing interests.

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