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CLINICAL TRIAL REPORT

Effect of Different Doses of Esketamine on Postoperative Recovery in Patients Undergoing Gynecologic Laparoscopic Surgery, a Randomized, Double-Blind, Single-Center Clinical Study

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Purpose: This study aimed to explore the effect of preoperative different doses of esketamine on postoperative recovery in patients undergoing gynecologic laparoscopic surgery.

Methods: A total of 99 women scheduled for gynecologic laparoscopic surgery under general anesthesia were enrolled and randomized. Three minutes before surgical incision, patients in the three groups were intravenously administered 0.25 mg/kg esketamine, 0.5 mg/kg esketamine, and an equivalent dose of saline, respectively. The primary outcome was the Quality of Recovery-15 (QoR-15) score assessed on 1 day (pod1), 3 days (pod3), and 7 days postoperatively (pod7). Secondary outcomes encompassed the VAS score, MAP, HR, frequency of rescue analgesia and length of hospital stay.

Results: Compared with group C, QoR-15 score was significantly improved in group E_1 and E_2 on pod1, while the rest VAS score was significantly decreased at 6h postoperatively (F =19.164, $P < 0.001$; $F = 6.059$, $P = 0.034$). On pod1, the VAS scores at rest and movement in group E_2 were significantly lower than those in group C ($P = 0.007$, $P = 0.038$). There was a significant decrease in resting VAS scores in the E_2 group compared with group C on pod3 ($P = 0.021$). Compared with group C, the QoR-15 score in group E_2 increased on pod7 ($P = 0.008$), but there was no clinical difference. There was no significant difference in MAP and HR among the three groups at each time point ($F = 0.758$, $P = 0.471$; $F = 0.232$, $P = 0.794$). There was a significant difference in the number of postoperative rescue analgesia among the three groups ($P = 0.023$).

Conclusion: Preoperative single small dose of esketamine can improve the quality of recovery 24h after gynecologic laparoscopic surgery patients, decrease the number of rescue analgesia, and may contribute to the rapid recovery of patients. And 0.5 mg/kg esketamine seems to be better.

Keywords: Esketamine, postoperative quality of recovery, gynecology, laparoscopic surgery

Introduction

Gynecologic laparoscopic surgery has become the main surgical method for gynecologic surgery due to its advantages such as less trauma, low postoperative infection rate, faster recovery time, and shorter hospital stay.[1,2] Although laparoscopic surgery is less painful than open surgery, about 20–40% of patients still experience moderate or even severe postoperative pain after laparoscopic surgery.[3] Post-laparoscopic surgery pain can be separated into incisional pain, shoulder-tip pain, and/or upper abdominal pain.[4,5] In addition, the stress response induced by preoperative anxiety, intraoperative pneumoperitoneum and postoperative pain not only stimulates the sympathetic nerves and triggers a series of stress responses but also may inhibit the gastrointestinal tract and immune function, and even affect the neuroendocrine function, leading to changes in postoperative

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mental and psychological state as well as internal environment disorders, which can seriously affect postoperative recovery.[6–8] Quality of recovery (QoR) after anesthesia is an important index to measure the early postoperative health status of patients.[9]

Currently, opioids are still the key drugs for postoperative analgesia due to their powerful analgesic effects.[10] However, the side effects associated with opioid analgesics, such as respiratory depression, nausea, vomiting, gastrointestinal paralysis, sleep disturbances, and pain hypersensitivity, will also affect the quality of the patient's postoperative recovery in varying degrees.[11–13] In order to minimize these side effects while catering to the multimodal analgesia in ERAS (Enhanced Recovery After Surgery). Non-opioid analgesics can be used as auxiliary analgesia to improve perioperative pain and accelerate the rapid recovery of patients after surgery.[14–16]

Esketamine is a highly active isomer of ketamine with a higher affinity for the aspartate receptor and opioid μ-receptor than that of ketamine. So it has a stronger analgesic effect and its anesthetic intensity is three to four times that of dextroketamine.[17] Esketamine can block the N-methyl-D-aspartic acid (NMDA) receptor noncompetitively when it enters the body. At the same time, it can change the structure of the receptor by allosteric action, which exerts the effects of anti-hyperalgesia, alleviating abnormal pain and increasing pain tolerance.[18,19] Esketamine has high clearance rate and fast metabolism in human body. It improves the controllability of anesthesia and makes patients wake up faster and safer.[20] Esketamine was originally used as a psychoactive drug to treat treatment-resistant depression. It has been reported to improve psychosocial functioning and prognosis in depressed patients.[21] In recent years, several studies have also begun to use esketamine to control postoperative pain and reduce opioid use. Low-dose esketamine (0.15 mg/kg~0.5 mg/kg) has been found to be effective in reducing postoperative opioid consumption and opioid-related side effects (nausea and vomiting) as an adjunct to multimodal analgesia regimens with fewer side effect.[22–25] Nielsen et al reported that intraoperative use of esketamine reduced postoperative pain and opioid use in patients undergoing spinal surgery.[26] Zhu et al reported that esketamine was effective in reducing postoperative depression in breast cancer patients without increasing the incidence of adverse events and improved the quality of postoperative recovery in breast cancer patients to some extent.[18] In addition, Qiu et al found the prophylactic effect of intraoperative esketamine (0.3 mg/kg/h) infusion on the incidence of postoperative sleep disturbance in patients who underwent gynecological laparoscopic surgery.[27]

However, there are no studies on whether perioperative use of esketamine helps to reduce postoperative pain and improve the quality of postoperative recovery in patients undergoing gynecologic laparoscopic surgery. Therefore, we hypothesize that esketamine can improve the quality of postoperative recovery in patients undergoing gynecological laparoscopic surgery and aim to determine the optimal dosage of esketamine to provide a reference for clinical practice.

Materials and Methods

Study Setting and Population

The trial was approved by the Ethics Committee of the Anhui No.2 Provincial People's Hospital (Ethics Approval Number: (R)2024–026 Anhui, China) and registered in the China Clinical Trial Registry (ChiCTR2400082718) on April 7, 2024. We enrolled 99 female patients who underwent laparoscopic gynecologic surgery under general anesthesia from April to August 2024. All patients received written informed consent. The inclusion criteria were as follows: Age 18 to 70 years; BMI (Body mass index): 18 to 30 kg/m^2; American Society of Anesthesiologists (ASA) physical status I–III; elective laparoscopic gynecologic surgery under general anesthesia; voluntary participation in this study and signed informed consent. Exclusion criteria included: allergy to the drugs used in this study; inability to communicate due to preoperative cognitive or language impairment; cardiac, hepatic or renal dysfunction; untreated or poorly controlled hypertension; glaucoma, elevated intracranial pressure, hyperthyroidism or alcohol abuse; contraindications to esketamine (atherosclerosis, coronary artery disease, cardiac insufficiency, pulmonary heart disease, pulmonary arterial hypertension, etc); Patients with serious intraoperative adverse reactions (eg intraoperative hemorrhage, etc) or receiving other clinical trials during follow-up were not be included in the final statistical analysis.

Randomization and Blinding

According to the method of random data table (http://www.randomization.com), 99 patients were randomly divided into three groups in a ratio of 1:1:1. The low-dose esketamine group (group E_1) received 0.25 mg/kg esketamine by intravenous injection 3 minutes before the surgical incision, the high-dose esketamine group (Group E_2) received 0.50 mg/kg esketamine at the same time, and the control group with an equal dose of saline (Group C). The patient's grouping was placed in an opaque sealed envelope. Upon entering the operating room, the envelope was opened by a separate nurse anesthetist who was not involved in the perioperative care of the patient or data collection. The study drug was prepared and provided to the anesthesiologist by the nurse anesthetist according to the grouping in the envelope. A 20 mL syringe containing 20 mL of 0.9% saline with or without esketamine (all esketamine used in this study was 2.5 mg/mL). However, the anesthesiologists and the statistician who were responsible for postoperative follow-up were not aware of the grouping of patients.

Anesthesia and Perioperative Care

None of the patients had any preoperative medication. After admission to the operating room, all underwent routine continuous monitoring (Myriad, Shenzhen, China), including BP (blood pressure), ECG (electrocardiography), SpO_2 (pulse oxygen saturation), and PSI (patient state index). Before anesthesia, the peripheral veins of the upper extremities were opened and balanced fluids were infused at a rate of 5–7 mL/kg/h until the induction of anesthesia. Anesthesia induction began 3 minutes after mask inhalation of pure oxygen. All patients in the three groups were injected intravenously with midazolam 0.05 mg/kg, sufentanil 0.4 ug/kg, etomidate 0.2 mg/kg, and rocuronium 1.0 mg/kg for anesthesia induction. Endotracheal intubation was performed after PSI value was 25–50 and muscle relaxation was satisfactory. Mechanical ventilation parameters were adjusted: respiratory rate 12~16 times/min, tidal volume of 6–8 mL/kg, and inspired oxygen flow 1–2 L/min to maintain the partial pressure of end-tidal carbon dioxide ($P_{et}CO_2$) 35–45 mmHg. Three minutes before skin incision, group E_1 was injected with esketamine (Jiangsu Hengrui Medicine) 0.25 mg/kg intravenously, group E_2 with esketamine 0.50 mg/kg intravenously, and group C was injected intravenously with an equal dose of saline. The nurse who did not participate in the anesthesia operation drew the drug or the normal saline diluted into 20 mL according to the patient's body weight. During the operation, propofol (4–8 mg/kg/h), remifentanil (0.1–0.3 ug/kg/min), and sevoflurane (1–2%) were injected intravenously continuously, and the patient's PSI value was maintained between 25 and 50. Cisatracurium (0.03 mg/kg) was given intermittently to maintain satisfactory intraoperative muscle relaxation. Intraoperatively, the patient's MAP and HR fluctuated within 20% of baseline, and vasoactive drugs were used as necessary. Sevoflurane was turned off, cisatracurium was not added, and sufentanil 0.1 μg/kg was injected intravenously in all three groups 30 min before the end of surgery. All anesthetic drugs were stopped at the time of skin suture, and flurbiprofen axaxl 50 mg and ondansetron 4 mg were intravenously injected in the three groups and then sent to the postanesthesia care unit (PACU). The endotracheal tube was removed when the patient awoke spontaneously and muscle strength returned. When the Steward score (mainly from the degree of consciousness, respiratory tract patency, and limb activity of the three indicators; each index is 0–2 points, with the highest score of 6 points) is greater than 4, patients can be sent back to the ward. If there were any special circumstances, a good handover should be made with the bedside doctors and nurses.

Data Collection

The primary outcome was the total QoR-15 (15-item Quality of Recovery) score based on QoR-15 scale on 1 day post-operatively (pod1), 3 days postoperatively (pod3), and 7 days postoperatively (pod7). The QoR-15 questionnaire evaluates the total QoR-15 score on the basis of physical comfort (5 items), emotional state (4 items), psychological support (2 items), physical independence (2 items), and pain (2 items). The total QoR-15 score ranges from 0 to 150, with higher scores indicating better quality of postoperative recovery.

At 1 h (a), 6 h (b), 1 day (c) and 3 days (d) after surgery, the Visual Analogue Score (VAS) pain scale (0, no pain; 10, the most severe pain) was used to evaluate the pain intensity at rest and movement after surgery; and whether rescue analgesia is required (flurbiprofen axetil 50 mg IV with a maximum dose of 200 mg when the postoperative VAS score is >4).

MAP and HR in each group were measured at baseline (t_1), 5 min after induction of anesthesia (t_2), 5 min after skin incision (t_3), and 5 min after the end of the surgery (t_4). Patients' general information (age, gender, BMI, ASA classification,

preoperative hemoglobin (Hb) content), intraoperative status (anesthesia and surgery duration, intraoperative propofol and remifentanil dosage), and duration of hospitalization were also collected.

Sample Size and Statistical Analysis

According to the first 15 patients in the pre-experiment, the mean total score of QoR-15 on the day after surgery in the three groups was 119.4, 123.8 and 126.2, respectively. The standard deviation (SD) were 5.2, 6.1 and 7.3, respectively. Setting a bilateral α=0.05, 1-β=0.9, and considering a 10% loss-to-follow-up rate. The sample size of each group was calculated to be 33 cases using PASS 15.0.

Statistical analysis was performed using the SPSS 27.0 software program. Numerical variables (age, BMI, time of extubation, length of hospital stay) were expressed as mean ± standard deviation ($\bar{x} \pm s$), anomaly distribution (hemoglobin, dosage of propofol and remifentanil, time of anesthesia and surgery) was expressed as median (25–75% percentile). If it was normal distribution and met the homogeneity test of variance, the one-way ANOVA test was used. If it did not meet the normal distribution, Kruskal–Wallis test was used. Categorical variables (hypertension, diabetes, type of surgery, nausea and vomiting, and remedial analgesia) were expressed as frequency (%) and analyzed using either the x^2 test or *Fisher's* exact test. Repeated measures ANOVA was used to compare different time points within the groups (such as MAP, HR, VAS score, QoR-15 score). $P < 0.05$ was considered statistically significant.

Results

Demographic and Clinical Characteristics of the Patients

A total of 99 patients were enrolled in the study. Of these, one patient in group C underwent laparotomy due to intraoperative surgical requirements, one patient in group E_1 had a delayed extubation because she had to wait in PACU for freezing results, and one patient in group E_2 was abruptly refused follow-up. Therefore, a total of 96 patients were finally completed and included in the statistical analysis according to the study protocol, with 32 patients in each group (Figure 1). The baseline data of patients in the three groups are listed in Table 1, and there was no statistical difference among the groups.

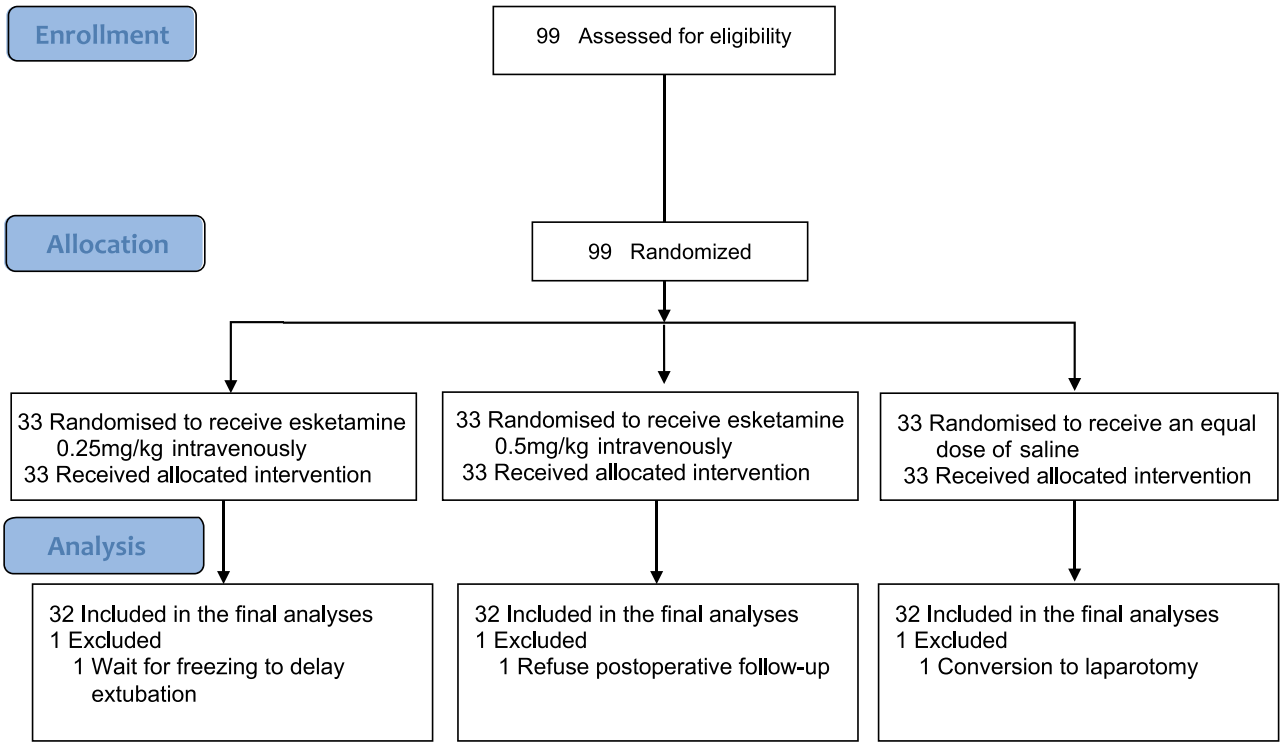

Figure 1 Consolidated Standards of Reporting Trials (CONSORT) flowchart describing patients' participation in the study.

Table 1 Basic Characteristics

Variables	Group C (n = 32)	Group E_1 (n = 32)	Group E_2 (n = 32)	*P* value
Ages, yr	50±11	46±11	47±10	0.287
Body mass index, kg/m^2	23.7±3.4	23.3±3.5	23.6±2.9	0.870
ASA physical status				0.227
I	3 (9.4)	7 (21.9)	3 (9.4)	
II	25 (78.1)	19 (59.4)	26 (81.2)	
III	4 (12.5)	6 (18.7)	3 (9.4)	
Hypertension	6 (18.7)	4 (12.5)	3 (9.4)	0.541
Diabetes mellitus	2 (6.3)	1 (3.1)	0 (0)	0.242
Hemoglobin, (g/L)	128 (119–135)	121 (109–130)	124 (112–130)	0.342
Types of surgery				0.673
Hysterectomy	17 (53.1)	13 (40.6)	18 (56.2)	
Hysteromyomectomy	4 (12.5)	8 (25.0)	6 (18.8)	
BSO	5 (15.6)	3 (9.4)	2 (6.2)	
Oophorocystectomy	6 (18.8)	8 (25.0)	6 (18.8)	

Notes: The data are expressed as means±SD, median (25th to 75th percentiles), or number of patients (percentage).
Abbreviations: ASA, American Society of Anesthesiologists; BSO, Bilateral Salpingo-oophorectomy.

Primary Outcome

On pod1, total QoR-15 scores were significantly higher in both group E_1 and E_2 than in group C (F = 19.164, P < 0.001 Table 2), whereas there was no statistically significant difference in total QoR-15 scores between groups E_1 and E_2 (P = 0.209). There was no significant difference in QoR-15 scores among the three groups on pod3 (F = 2.729, P = 0.071). Compared with

Table 2 QoR-15 Scores at Different Time Points in the Three Groups

Variables	Group C (n = 32)	Group E_1 (n = 32)	Group E_2 (n = 32)	*F* Value	*P* value
pod1	105.22±15.14	112.75±7.00*	114.81±8.11*	19.164	<0.001
pod3	120.69±6.00[a]	123.16±6.21[a]	124.28±6.64[a]	2.729	0.071
pod7	131.50±5.84[ab]	132.88±4.93[ab]	135.06±4.79*[ab]	3.783	0.026
F	254.921	159.194	170.350		
η^2	0.847	0.776	0.787		
P value	<0.001	<0.001	<0.001		
Overall test					
Within-group	*F* =10.479	η^2 =0.184	*P* <0.001		
Between-group	*F* =676.516	η^2 =0.879	*P* <0.001		
Interaction	*F* =7.053	η^2 = 0.132	*P* <0.001		

Notes: *Indicates P <0.05 compared with group C at the same time point; [a]Indicates P < 0.05 compared with pod1 in each group; [b]Indicates P < 0.05 compared with pod3 in each group. Comparisons between groups were corrected by Bonferroni test.
Abbreviations: QoR-15 score, 15-item Quality of Recovery; pod1, 1 day postoperatively, pod3, 3 days postoperatively; pod7, 7 days postoperatively.

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group C, the QoR-15 score in group E_2 increased on pod7 ($P = 0.008$). Compared with the pod1, the total QoR-15 scores in the three groups increased significantly with time on pod3 and pod7 ($F = 254.921$, $\eta^2 = 0.847$, $P < 0.001$; $F = 159.194$, $\eta^2 = 0.776$, $P < 0.001$; $F = 170.350$, $\eta^2 = 0.787$, $P < 0.001$).

Secondary Outcomes

The VAS Scores During 1 h, 6 h, 1 day and 3 days After Surgery

Compared with group C, both group E_1 and group E_2 had a significant decrease in resting VAS scores at 6h post-operatively ($F = 6.059$, $P = 0.034$, Figure 2). On 1 day postoperatively, the VAS scores at rest and movement in group E_2 were significantly lower than those in group C ($P = 0.002$, $P = 0.013$). There was a significant decrease in resting VAS scores in the E_2 group compared with group C on 3 days postoperatively ($P = 0.021$).

Comparison of Perioperative MAP and HR Among Three Group

We statistically analyzed the perioperative hemodynamic parameters of patients in the three groups, as shown in Figure 3. There was no significant difference in MAP and HR among the three groups at each time point ($F = 0.758$, $P = 0.471$; $F = 0.232$, $P = 0.794$).

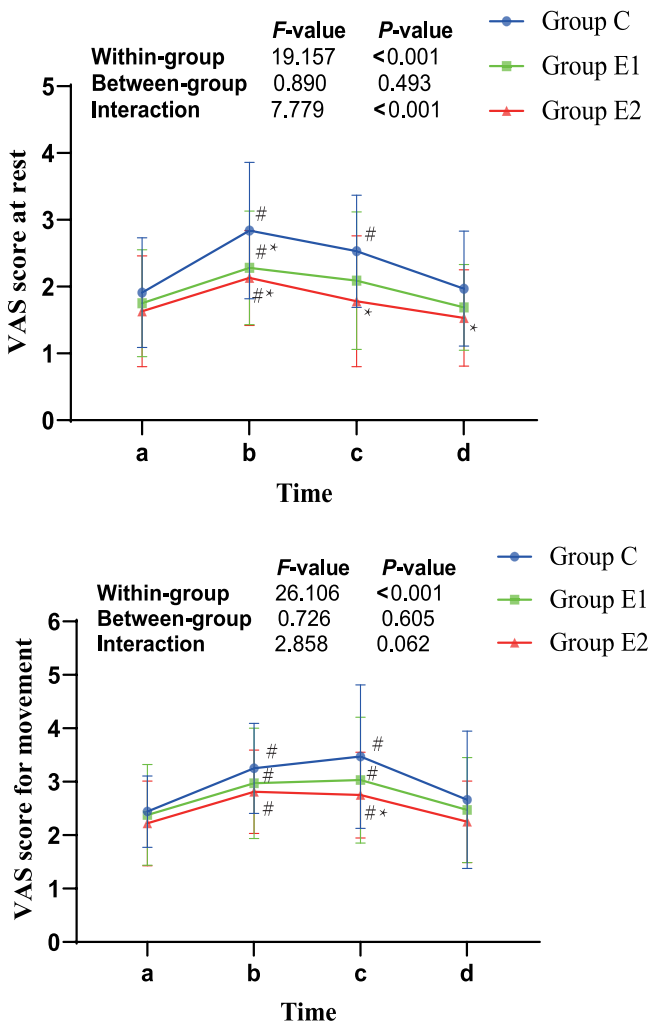

Figure 2 VAS scores at different time points in the three groups. *Indicates $P < 0.001$ compared with group C at the same time point; #Indicates $P < 0.001$ compared with a in each group.

Abbreviations: VAS, Visual Analogue Score; a, 1 h after surgery; b, 6 h after surgery; c, 1 day after surgery; d, 3 days after surgery.

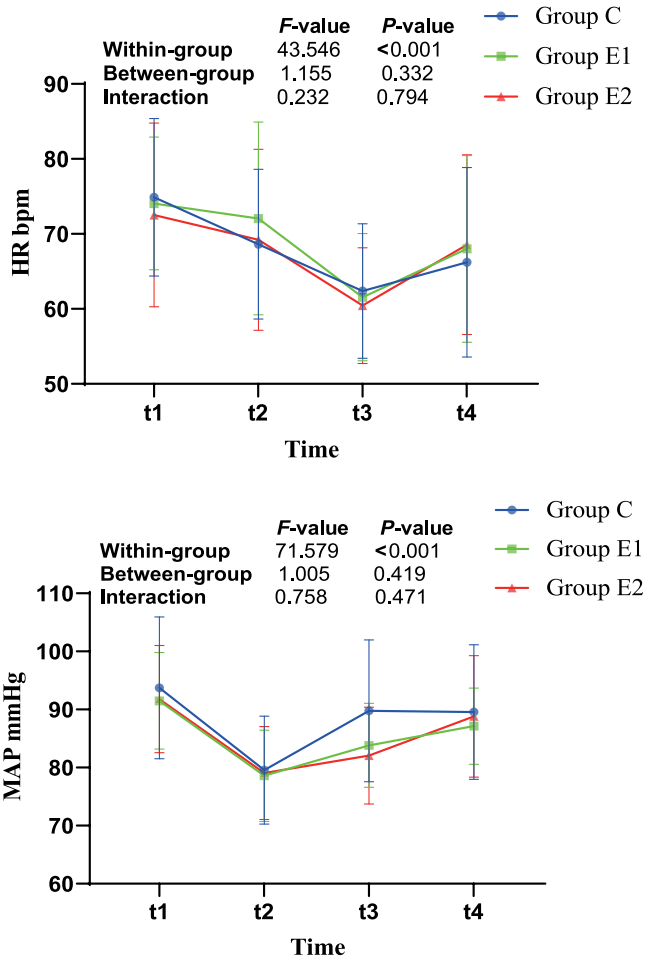

Figure 3 Vital signs at different time points in the three groups. t_1: at baseline; t_2: 5 min after induction of anesthesia; t_3: 5 min after skin incision; t_4: 5 min after the end of the surgery.

Comparison of Perioperative Surgery-Related Parameters Among Three Groups

We also analyzed the perioperative surgery-related parameters among the three groups. And it was found that there were no statistical differences in perioperative propofol dosage, remifentanil dosage, anesthesia time, surgery time, extubation time and duration of hospitalization among the three groups (Table 3). At the same time, the perioperative adverse events in the three groups of patients were statistically analyzed. It can be seen that no-intraoperative consciousness occurred in

Table 3 Perioperative Relevant Parameters

Variables	Group C (n = 32)	Group E_1 (n = 32)	Group E_2 (n = 32)	*P* value
Propofol dosage, mg	342.50 (287.5–453.13)	345.00 (287.50–483.33)	331.67 (266.67–405.00)	0.574
Remifentanil dosage, mg	0.88 (0.72–1.16)	0.88 (0.71–1.21)	0.85 (0.68–1.01)	0.572
Anesthesia time, min	107.50 (80.00–130.00)	108.05 (90.00–145.00)	100.00 (85.00–121.50)	0.597
Surgical time, min	80.00 (60.25–110.00)	86.00 (70.50–125.00)	77.50 (65.50–103.75)	0.568
Extraction time, min	14.66±8.60	12.59±6.48	15.75±10.09	0.327
Length of hospital stay, day	9.88±4.09	9.13±2.94	9.63±3.60	0.695

(*Continued*)

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Table 3 (Continued).

Variables	Group C (n = 32)	Group E_1 (n = 32)	Group E_2 (n = 32)	*P* value
Intraoperative awareness	0	0	0	1.000
Nausea and vomiting	6 (18.8)	7 (21.9)	9 (28.1)	0.662
Remedial analgesia	8 (25)	3 (9.4)	1 (3.1)	0.023
Hallucinations	0	0	0	1.000

Notes: The data are expressed as means±SD, median (25th to 75th percentiles), or number of patients (percentage).

the three groups. There was no significant difference in the incidence of postoperative nausea and vomiting among the three groups ($P = 0.662$). A total of 8 patients in group C needed remedial analgesia during the perioperative period, 3 in group E_1 and 1 in group E_2, the difference being statistically significant ($P = 0.023$).

Discussion

The results of this study suggest that for patients undergoing laparoscopic gynecologic surgery, esketamine was given intravenously (0.25 mg/kg or 0.50 mg/kg) before skin incision compared to the control group significantly improved the quality of recovery on 1 day postoperatively. Although there was a significant difference in QoR-15 scores between 0.50 mg/kg esketamine group and control group on 7 days postoperatively, there was no clinical difference. Intravenous injection of esketamine before skin incision can also decreased patients' resting VAS score at 6h postoperatively reduced the number of postoperative rescue analgesia, and did not increase the occurrence of postoperative adverse reactions. This study also found that intravenous injection of esketamine 0.5 mg/kg before incision could also reduce the rest and movement VAS scores of patients on 1 day after surgery. Compared with the control group, 0.50 mg/kg esketamine group improved the rest VAS score on 3 days after surgery.

In recent years, with the development of minimally invasive technology, and anaesthetist pay more and more attention to postoperative analgesia and multimodal analgesia. Although the tissue damage of laparoscopic surgery is very limited and confined to the intraoperative period,[28] most patients undergoing gynecologic laparoscopic surgery experience acute pain after surgery. Postoperative acute pain not only prolongs the time for patients to get out of bed but also affects the rapid recovery after surgery.[29] Acute pain, if not properly controlled, can develop into chronic pain. It affects the patient's quality of life.[30] In this study, we found that intravenous esketamine injection before surgery reduced the resting VAS scores at 6h after surgery, improved the QoR-15 score on 1 day after surgery, and reduced the number of postoperative remedial analgesia compared with the control group. In addition, 0.50 mg/kg esketamine improved the rest and movement VAS scores on 1 day after surgery, and rest VAS scores on 3 days after surgery. This is somewhat similar to the results of previous studies.[31–33] However, there was no clinical difference in the movement VAS scores among the three groups on the 3 days after surgery and QoR-15 scores on 3 days and 7 days after surgery in this study. This may be because, first of all, laparoscopic surgery was selected in this study, which is relatively less invasive than open surgery. Secondly, previous studies continued to pump esketamine intraoperatively, whereas in this study we only administered it during induction, which may have resulted in a limited duration of esketamine. In addition, the resting and moving VAS scores were performed separately in this study, while only rough VAS scores were performed in previous studies. Finally, the difference in QoR-15 scores among the groups on 3 days after surgery in previous studies was small (<6, MCID-minimal clinically important difference),[34] and whether it has clinical significance may need to be demonstrated by further clinical studies.[18] Although the use of esketamine in this study only improved resting VAS scores at 6 h and 3 days after surgery, it still suggests that esketamine may help to accelerate the recovery of intestinal function after surgery, alleviate the sleep disorder and appetite loss caused by pain, and may help patients get out of bed early, reduce pulmonary complications, and improve the comfort and recovery quality of patients.

This study also found that intravenous esketamine injection before surgery reduced the number of postoperative remedial analgesia compared with the control group. This may be because esketamine, which acts as an NMDA receptor antagonist and inhibits the NMDA receptor, binds to the μ-opioid receptor,[35,36] increases the concentration of

5-hydroxytryptamine and norepinephrine in the brain.[37] This prevents activation of the nociceptive system in opioid-related injuries and weakens opioid tolerance and nociceptive hypersensitivity.[38] And its intravenous effect was dose-dependent.[39] In addition, S-norketamine is an active metabolite converted from esketamine in vivo. And its anesthetic effect is 1:5 to 1:3 that of esketamine, with an elimination half-life of 6–10 h, which may also be related to the longer analgesic time of ketamine.[40,41] This is consistent with the findings in this study that intravenous esketamine 0.5 mg/kg was more effective than 0.25 mg/kg before skin incision. Although the analgesic effect of esketamine was dose-dependent.[39] Considering that it has dose-dependent adverse reactions at the same time, that is, lower dose may allow for better tolerability while maintaining efficacy.[42,43] Therefore, low-dose of esketamine was selected for the preliminary exploratory trial in this study. Similarly, intravenous infusion of 0.20 mg/kg or 0.40 mg/kg esketamine has been shown to have an antidepressant effect.[42] This suggests that esketamine may improve the quality of postoperative recovery through its antidepressant effect in this study.

In addition, one study found that postoperative pain did not improve in patients who were given esketamine after surgery compared to those who were given esketamine before surgery.[23] This suggests that the timing of esketamine treatment also plays a crucial role in its analgesic effect. This was why we chose to inject esketamine intravenously before the start of surgery in this study. On the one hand, excessive anesthetic drugs were avoided during the induction period, which would cause the hemodynamics of patients to drop sharply. On the other hand, esketamine played the preventive analgesic effect, effectively inhibited the stress response during the surgery and did not affect the patient's postoperative extubation time. In previous studies, it was believed that the intraoperative use of esketamine could reduce the dosage of remifentanil.[44] However, we did not find any difference in the dose of remifentanil among the three groups in this study. This may be due to the fact that in previous studies, a load dose of esketamine was administered first, followed by continuous pumping until the end of surgery. Considering this may prolong the postoperative extubation time of patients. We only used a single intravenous injection. Thus, in this study, intravenous administration of esketamine before the start of surgery helped to improve the quality of patients' postoperative recovery and did not prolong the postoperative extubation time.

Finally, this study also has some limitations. First, the main purpose of this study was to observe the effect of a single intravenous injection of different doses of esketamine on the quality of postoperative recovery in gynecologic laparoscopic surgery patients. And the calculation of sample size was mainly based on the quality of postoperative recovery score. Our relatively small sample size, and single-center design may lead to imperfect observation of secondary indicators such as postoperative adverse events and dosage of anesthetic drugs. Therefore, subsequent trials with larger sample size are still needed for observation. Second, the administration of esketamine in this study was a single intravenous injection, and its blood concentration was not as stable as that of intravenous pumping. We will further improve it in future studies. Finally, due to time constraints and patients' compliance with the scale, we observed quality of recovery only 7 days after surgery. The effect of different doses of esketamine on the quality of long-term recovery after gynecologic laparoscopic surgery remains to be further studied.

Conclusions

Preoperative single small dose of esketamine can improve the quality of recovery 24h after gynecologic laparoscopic surgery patients, decrease the number of rescue analgesia, and may contribute to the rapid recovery of patients. And 0.50 mg/kg esketamine seems to be better.

Data Sharing Statement

The datasets generated and analyzed during the current study are available from the corresponding author on reasonable request.

Ethics Approval

This study was performed in line with the principles of the Declaration of Helsinki and was registered in the China Clinical Trial Registry (ChiCTR2400082718). The study protocol was approved by the Research Ethics Committee for

Experimental and Clinical Studies at Anhui No.2 Provincial People's Hospital, China [Ethics approval number: (R)2024-026 Anhui, 7 April, 2024].

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Disclosure

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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