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CLINICAL TRIAL REPORT

Intraoperative Administration of Esketamine is Associated with Reduced Opioid Consumption After Laparoscopic Gynecological Surgery: A Randomized Controlled Trial

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Purpose: To explore the postoperative opioid-sparing effect and incidence of adverse events of different dosages of intraoperative esketamine administration in patients undergoing laparoscopic gynecological surgery.

Patients and Methods: Patients undergoing elective gynecological laparoscopic operation was enrolled and randomly allocated to lower-dose esketamine group, higher-dose esketamine group, or control group. Patients in the two intervention groups received esketamine doses of 0.25 mg/Kg and 0.50 mg/Kg before wound incision. Subsequently, maintenance doses of 0.20 mg/Kg/h and 0.40 mg/Kg/h were administered throughout the procedure, respectively. The control group was given an intravenous injection and a maintenance infusion of normal saline. A patient-controlled analgesia (PCA) intravenous pump containing sufentanil was connected to control postoperative pain. Rescue analgesia was provided with injection of tramadol 100 mg.

Results: In total, 120 subjects were included in data analysis. The 24 hours and 48 hours PCA opioid consumption, 24 hours and 48 hours cumulative opioid in both lower-dose and higher-dose esketamine groups were lower than those in the control group. However, postoperative opioid consumption was comparable between the two intervention groups. No differences were found in extubation time, acute postoperative pain intensity, and incidence of adverse effects among the three groups.

Conclusion: Intraoperative esketamine administration at both low and high doses reduces opioid consumption after gynecological laparoscopic surgery, without increasing the risk of adverse events.

Keywords: esketamine, opioids, postoperative pain, gynecological laparoscopic surgery

Introduction

Although laparoscopic surgery causes less pain than open procedure, opioids are still indispensable for perioperative pain control.[1] However, opioids commonly induce several adverse events including nausea, vomiting, pruritus and respiratory depression.[2,3] Furthermore, postoperative opioid medication might cause opioid addiction.[4,5] Opioid dependence frequently follows surgical procedure, so it can have long-term benefit to control postoperative pain with opioid-sparing strategies.[6,7]

Ketamine blocks N-methyl-D-aspartic acid receptor (NMDA) receptor uncompetitively, so as to prevent acute pain.[8] It can be served as an adjunct for perioperative multimodal analgesia.[9,10] Ketamine can also prevent hyperalgesia and persistent pain since NMDA receptor plays a critical role in the plasticity regulation.[11,12] Numerous published data have proven that ketamine can reduce postoperative pain intensity and opioid requirement, making it an alternative agent for the opioid-sparing strategy.[10,13–15] However, psychotomimetic adverse effects like hallucinations and dizziness have limited the usage of racemic ketamine in clinical practice.[16]

As the S-enantiomer of ketamine, esketamine has been shown to have twice the potency of racemic ketamine in analgesia and a lower incidence of adverse events.[17,18] However, data are scarce regarding the effects of esketamine use during surgery

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on postoperative opioid requirement, and pain following laparoscopic gynecological surgery. Moreover, the optimal dose of esketamine for this indication has not yet been clear since few multi-dose studies have been conducted.

Therefore, we carried out the present trial to explore the postoperative opioid-sparing effect of two dosages of esketamine in patients undergoing gynecological laparoscopic surgery. Moreover, we sought to determine the safety profile of intraoperative esketamine administration in this population subset.

Materials and Methods

Study Design

This randomized controlled trial was reviewed and approved by the Ethics Committee of The First Affiliated Hospital of Chongqing Medical University (No. 2022–229) and registered on the Chinese Clinical Trial Registry prior to initiation (www.chictr.org.cn, No. ChiCTR2300073287). All subjects signed informed consent forms. The study report was in accordance with the Consolidated Standards of Reporting Trials (CONSORT) checklist.[19] This clinical trial complied with the Declaration of Helsinki.

The subjects scheduled for elective laparoscopic gynecological operation under general anesthesia were enrolled between 17/07/2023 and 01/12/2023. We included patients aged 18–65 with American Society of Anesthesiologists (ASA) physical status I to II. The exclusion criteria included body mass index (BMI) > 35 Kg/m², psychiatric disease, hyperthyroidism or pheochromocytoma, increased intracranial or intraocular pressure, uncontrolled hypertension, severe hepatorenal insufficiency, pregnancy, lactation, preoperative opioid medication, an inability to rate pain intensity with numerical rating scale (NRS). Participants whose procedures took >4.5 hours or those with surgeries converted from laparoscopic to open approach were excluded from pre-protocol (PP) analysis.

Randomization and Blinding

The subjects were assigned to 3 groups randomly in a ratio of 1:1:1 ratio according to a list of randomization generated in SPSS 25.0 (IBM, Chicago, IL, USA). A researcher blinded to patients conducted random assignment by preparing sealed and coded opaque envelopes for concealment. Simultaneously, emergency envelopes containing medication name and number of the case were prepared to enable the unblinding when necessary.

On the surgical day, a nurse who was blinded to the patient's care opened an envelope containing subjects' assignment information, prepared study drugs in a separated room. The study agents were diluted with 0.9% NaCl solution to two syringes (a 5-mL and a 50-mL) which appeared identical. The syringes were labeled with "study drugs" and patients' number.

Prior to the skin incision, the control group received a loading dose of normal sodium (0.9% NaCl) intravenously, followed by 0.9% NaCl solution infusion throughout the procedure. The lower-dose esketamine group was given a loading dose of esketamine (0.25 mg/Kg) intravenously before wound incision and a maintenance dose of esketamine 0.2 mg/Kg/h. The higher-dose group was given a loading dose of esketamine (0.5 mg/Kg) intravenously and a maintenance dose of esketamine 0.4 mg/Kg/h.

The responsible anesthesiologist delivered the loading dose by the 5-mL syringe and the maintenance dose by the 50-mL syringe (0.1 mL/Kg/h) till the end of surgery.

Anesthesiologists, surgeons, anesthesia nurses, surgical nurses, patients and researchers evaluating outcome variables were blinded to patients' allocation.

Anesthesia Management

Patients were introduced to an 11-point NRS for pain assessment and to a proper patient-controlled analgesia (PCA) device use preoperatively. All subjected fasted from solid foods for 8 hours and from clear fluids for 2 hours before surgery. On their admission in operating room, electrocardiography (ECG), pulse oxygen saturation (SpO_2), heart rate (HR), non-invasive blood pressure (NIBP), bispectral index (BIS), and capnography were monitored continuously.

Anesthesia induction was conducted with injection of midazolam 0.02–0.05 mg/Kg, propofol 1.5–2.0 mg/Kg, sufentanil 0.3–0.5 μg/Kg and vecuronium 0.1 mg/Kg. Following tracheal intubation, mechanical ventilation was initiated

and end-tidal carbon dioxide partial pressure ($P_{ET}CO_2$) was kept at 35–45 mmHg. Anesthesia was maintained with infusions of propofol and remifentanil, as well as inhalation of sevoflurane. Vecuronium was administered intermittently as needed.

The intravenous infusion rates of propofol and remifentanil were adjusted by the responsible anesthesiologist to keep the mean arterial pressure (MAP) between 80% and 120% of baseline values and BIS value at 40–60 during surgery. At an appropriate anesthesia depth, a bolus of urapidil was injected when the MAP was evaluated by >20% of baseline values or was >90 mmHg. Hypotension, defined as MAP reduction by >20% of baseline values or <60 mmHg, was treated with additional fluid administration and a bolus injection of phenylephrine. Esmolol was injected when HR was >120 bpm, while atropine was administered when HR was <50 bpm.

No local or regional anesthesia was applied. All surgical procedures were conducted by a single surgical team. Pneumoperitoneum inflation pressure ranged from 10 to 12 mmHg.

All patients received dexamethasone 7 mg before induction of general anesthesia and tropisetron 2 mg at the end of wound closure for the prophylaxis of postoperative nausea and vomiting (PONV). Parecoxib 40 mg was given intravenously 20 min before the end of wound closure. Once skin closure was completed, remifentanil and propofol were discontinued, and flumazenil was injected intravenously. Neostigmine and atropine were given to antagonize the residual effects of neuromuscular blocking agents. After extubation, all subjects were transported to the postanesthesia care unit (PACU).

The patients were assessed for intensity of pain by a nurse blinded to the protocols in PACU. In case of NRS > 3, intravenous sufentanil titration using a 3-μg bolus every 15 minute was performed. Once the NRS score was ≤3, PCA was provided with intravenous sufentanil set to a bolus size of 0.05 μg/Kg, lock-out time of 10 minutes, and a maximum of five boluses per hour. Patients with Steward score of ≥4 were delivered to the surgical ward.

Postoperative Management

On the ward, flurbiprofen 50 mg was administered intravenously twice daily. The duration of PCA treatment was 48 hours. Intravenous tramadol 100 mg was administered as rescue analgesia when the NRS score was >3. PONV were treated with tropisetron and droperidol if necessary. Psychotomimetic adverse effects including nightmares, hallucinations, dizziness and diplopia were evaluated and were treated according to hospital service guidelines.

Outcome Measures

The primary outcome was 24 hours postoperative PCA opioid consumption. Opioid consumption was converted to morphine milligram equivalent (MME) units.

Secondary outcomes included rate of sufentanil administration in PACU; rate of rescue tramadol administration; 48 hours PCA opioid consumption; 24 hours and 48 hours postoperative cumulative opioid consumption including sufentanil injected in PACU, PCA sufentanil administration, and tramadol injected for rescue analgesia; the NRS pain scores during rest and cough at 1, 2, 4, 12, 24, 36 and 48 hours postoperatively; time to extubation; PACU length of stay; the incidence of psychotomimetic and opioid-related adverse effects; postoperative length of hospital stay. The occurrences of psychotomimetic and opioid-related adverse effects (nausea, vomiting, respiratory depression, pruritus and urinary retention) were recorded as dichotomous data (yes/no) by active questioning up to 48 hours.

Statistical Analysis

Sample size calculation was performed (One-way ANOVA, $\alpha = 0.05$, $1-\beta = 0.8$) to detect a 30% reduction in PCA sufentanil consumption during 24 hours postoperatively. Based on the study by Ithnin et al, the mean (standard deviation, SD) 24 hours MME consumption in gynecological surgery patients was 21.0 (11.4) mg, 35 subjects per group and a total of 105 subjects would be required. Additionally, four subjects were added to each group for possible loss to follow-up during the study. The PASS 15.0 software was used for sample size calculation. Patients were primarily analyzed within the groups to which they were allocated and received designated treatment, excluding those with conversion from laparoscopic surgery to laparotomy or surgical time of >4.5 hours (per-protocol population). For the primary outcome,

analysis was also performed in the intention-to-treat (ITT) population, based on whether or not the designated treatment was received and the primary outcome was evaluated.

The Kolmogorov–Smirnov normality test was taken to evaluate data distribution. Continuous data were shown as mean (SD) or median (interquartile range, IQR), as appropriate. Differences among groups were calculated using one-way ANOVA or the Kruskal–Wallis test according to the normality of distribution. The intervention groups were further compared to placebo group by Independent-Samples *T*-test or Mann–Whitney *U*-tests. As this procedure could be interpreted as a multiple comparison, the Bonferroni correction was applied. Categorical variables were presented as number (proportion) and were compared by chi-square test. *P*-values <0.05 were considered statistically significant. Statistical analysis was carried out using SPSS 25.0.

Results

Patient Inclusion and Characteristics

In total, 150 patients were evaluated in our study. As 24 patients were excluded before allocation, 126 patients were assigned to 3 groups randomly. Three patients in the lower-dose esketamine group, 2 patients in the higher-dose esketamine group and 1 patient in the control group dropped out from the study during follow-ups, respectively. Ultimately, data from 120 patients were analysed (Figure 1). Demographic characteristics, surgical and anesthesia variables were comparable among the groups (Table 1).

Primary Outcome

As Table 2 shows, the 24 hours postoperative PCA opioid consumption (in MME) in both lower-dose and higher-dose esketamine groups were lower when compared to the control group (lower-dose esketamine group vs control group, $P = 0.011$; higher-dose esketamine group vs control group, $P < 0.001$). However, no differences were shown between the

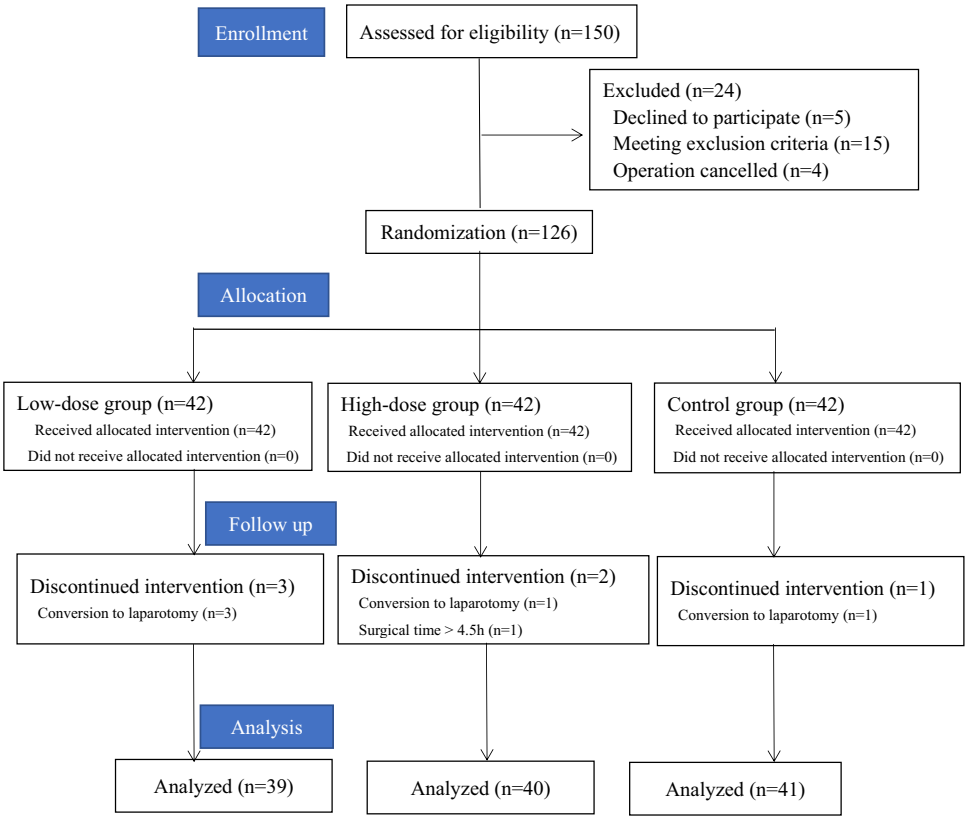

Figure 1 Consort flow diagram.

Table 1 Demographic Characteristics, Surgical and Anesthesia Variables of the Patients

Characteristics	Low-dose Esketamine Group (n=39)	High-Dose Esketamine group (n=40)	Control Group (n=41)	Overall Significance (*P*-value)
Age (mean ± SD, y)	49±8	49±7	48±9	0.624
Height (mean ± SD, cm)	157±4	158±4	157±4	0.551
Weight (mean ± SD, Kg)	59±9	61±7	58±7	0.129
BMI (mean ± SD, Kg/m^2)	23.9±3.4	24.5±2.8	23.2±2.5	0.163
ASA physical status, n (%)				0.443
I	13 (33.3%)	17 (42.5%)	12 (29.3%)	
II	26 (66.7%)	23 (57.5%)	29 (70.7%)	
History of pelvic surgery, n (%)	7 (17.9%)	6 (15.0%)	8 (19.5%)	0.863
Type of surgery, n (%)				0.919
Hysterectomy	21 (53.8%)	24 (60.0%)	19 (46.3%)	
Myomectomy	8 (20.5%)	9 (22.5%)	8 (19.5%)	
Adnexectomy	7 (17.9%)	5 (12.5%)	9 (22.0%)	
Endometriosis surgery	2 (5.1%)	1 (2.5%)	3 (7.3%)	
Other	1 (2.6%)	1 (2.5%)	2 (4.9%)	
Surgical time (mean ± SD, min)	114±43	128±51	116±38	0.287
Anesthesia time (mean ± SD, min)	142±44	160±52	152±39	0.214
Propofol during surgery (mean ± SD, mg/Kg·h)	2.8±0.7	2.7±0.6	2.9±0.6	0.319
Remifentanil during surgery (mean ± SD, μg/Kg·h)	6.9±1.5	7.2±1.4	7.0±1.5	0.617
Patients receiving vasoactive agents, n (%)				
Urapidil	2 (5.1%)	2 (5.0%)	2 (4.9%)	0.999
Phenylephrine	7 (17.9%)	7 (17.5%)	10 (24.4%)	0.686
Esmolol	1 (2.6%)	2 (5.0%)	2 (4.9%)	0.830
Atropine	3 (7.7%)	3 (7.5%)	5 (12.2%)	0.709
Intraoperative fluid infusion (median, IQR, mL)	1100 (1100, 1600)	1100 (1100, 1600)	1100 (1100, 1600)	0.476
Blood loss (median, IQR, mL)	100 (50, 150)	100 (50, 150)	100 (50, 150)	0.615
Urine output (mean ± SD, mL)	150 (120, 200)	150 (110, 200)	160 (150, 200)	0.543
Time to extubation (mean ± SD, min)	25±11	24±9	22±8	0.261
PACU length of stay (mean ± SD, min)	60±9	60±8	58±10	0.395
Postoperative length of stay (mean ± SD, d)	5±3	5±2	5±2	0.976

Abbreviations: SD, Standard deviation; BMI, body mass index; ASA, American Society of Anesthesiologists.

Table 2 Postoperative Opioid Consumption

	Low-Dose Esketamine Group (n=39)	High-Dose Esketamine Group (n=40)	Control Group (n=41)	Overall Significance (*P*-value)
Sufentanil administration in PACU, n (%)	13 (33.3%)	14 (35.0%)	18 (56.1%)	0.573
PCA MME consumption (mean ± SD, 95% CI)				
0–24h	47.6±22.9 (40.2, 55.1)*	41.6±16.3 (36.4, 46.8)*	58.7±17.9 (53.0, 64.3)	<0.001
24–48h	33.8±17.9 (28.0, 39.6)*	29.2±11.6 (25.5, 32.9)*	44.0±16.0 (39.0, 49.1)	<0.001
0–48h	81.5±38.4 (69.1, 93.9)*	70.8±26.8 (62.2, 79.4)*	102.7±31.9 (92.7, 112.8)	<0.001
Rescue tramadol administration, n (%)				
0–24h	8 (20.5%)	7 (17.5%)	11 (26.8%)	0.582
24–48h	4 (10.3%)	4 (10.0%)	4 (9.8%)	0.997
0–48h	10 (25.6%)	7 (17.5%)	11 (26.8%)	0.561

(*Continued*)

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Table 2 (Continued).

	Low-Dose Esketamine Group (n=39)	High-Dose Esketamine Group (n=40)	Control Group (n=41)	Overall Significance (*P*-value)
Postoperative cumulative MME (mean ± SD, 95% CI)				
0–24h	51.1±26.2 (42.6, 59.6)*	46.8±23.1 (39.4, 54.2)*	64.0±23.6 (56.6, 71.5)	0.005
24–48h	34.9±19.2 (28.6, 41.1)*	30.5±14.0 (26.0, 34.9)*	45.0±17.2 (39.6, 50.4)	0.001
0–48h	85.9±42.2 (72.2, 99.6)*	77.2±36.0 (65.7, 88.8)*	109.0±38.1 (97.0, 121.1)	0.001

Note: *$P < 0.05$ vs Control group.
Abbreviations: PACU, postanesthesia care unit; PCA, patient-controlled analgesia; MME, morphine milligram equivalent; SD, standard deviation; CI, confidence interval.

lower-dose and the higher-dose esketamine groups ($P = 0.164$). The ITT analysis results were consistent with those from the PP analysis for the primary outcome measures (lower-dose: 47.9±22.4; higher-dose: 43.8±19.4; control: 58.7±17.7; $P = 0.003$); it did not differ between the two treatment groups ($P = 0.346$).

Second Outcomes

Postoperative Analgesic Requirement

The rate of sufentanil administration in PACU and rate of rescue tramadol administration were comparable among the three groups. The 48-hour PCA opioid consumption, 24 hours and 48 hours cumulative opioid consumption were lower in the lower-dose and higher-dose esketamine groups when compared to control group ($P < 0.05$). However, no differences were shown between the two intervention groups on postoperative MME consumption (Table 2).

Postoperative Acute Pain Intensity

Intensity of postoperative acute pain during rest and cough are presented in Table 3. The NRS scores during rest and on cough at 1, 2, 4, 12, 24, 36 and 48 hours postoperatively were similar among the three groups.

Table 3 Postoperative Pain Intensity

	Low-Dose Esketamine Group (n=39)	High-Dose Esketamine Group (n=40)	Control Group (n=41)	Overall Significance (*P*-value)
Pain scores at rest (median, IQR)				
1h	2 (1, 2)	2 (1, 2)	2 (1, 2)	0.801
2h	2 (2, 3)	2 (2, 3)	2 (2, 3)	0.253
4h	2 (2, 3)	2 (2, 3)	2 (2, 3)	0.573
12h	2 (2, 3)	2 (2, 3)	2 (2, 3)	0.801
24h	2 (1, 2)	2 (1, 3)	2 (1, 2)	0.504
36h	2 (1, 2)	2 (1, 2)	2 (1, 2)	0.312
48h	1 (1, 1)	1 (1, 2)	1 (1, 1)	0.268
Pain scores during cough (median, IQR)				
1h	3 (3, 4)	3 (3, 4)	3 (3, 4)	0.471
2h	4 (4, 5)	4 (4, 5)	4 (3, 4)	0.095
4h	4 (3, 5)	4 (3, 4)	4 (3, 4)	0.279
12h	4 (3, 4)	4 (3, 4)	4 (3, 5)	0.209
24h	3 (3, 4)	3 (3, 4)	4 (3, 4)	0.152
36h	3 (2, 4)	3 (2, 4)	3 (3, 4)	0.673
48h	2 (2, 3)	2 (2, 3)	3 (2, 3)	0.093

Abbreviations: SD, standard deviation.

Table 4 Postoperative Adverse Effects

	Low-dose Esketamine Group (n=39)	High-Dose Esketamine Group (n=40)	Control Group (n=41)	Overall Significance (*P*-value)
Psychotomimetic adverse effects, n (%)				
Nightmares	0 (0)	0 (0)	2 (4.9%)	0.141
Hallucinations	0 (0)	0 (0)	0 (0)	/
Dizziness	3 (7.7%)	2 (5.0%)	0 (0)	0.216
Diplopia	0 (0)	0 (0)	0 (0)	/
Overall	3 (7.7%)	2 (5.0%)	2 (4.9%)	0.834
Opioid-related adverse effects, n (%)				
Nausea	10 (25.6%)	8 (20.0%)	13 (31.7%)	0.484
Vomiting	3 (7.7%)	1 (2.5%)	4 (9.8%)	0.404
Respiratory depression	1 (2.6%)	0 (0)	1 (2.4%)	0.601
Pruritus	1 (2.6%)	1 (2.5%)	2 (4.9%)	0.794
Urinary retention	0 (0)	1 (2.5%)	0 (0)	0.365
Overall	12 (30.8%)	9 (22.5%)	15 (36.6%)	0.381

Postoperative Recovery

There were no differences in extubation time, PACU length of stay, or length of postoperative hospital stay among the three groups (Table 1).

Postoperative Adverse Effects

As shown in Table 4, no difference was detected among the groups in the incidences of opioid-related or psychotomimetic adverse effects following surgery. Furthermore, the differences were insignificant between the two dosage groups. No differences were significant in the comparison between lower-dose and control groups or between higher-dose and control groups.

Discussion

The major finding of this study was that low and high doses of intraoperative infusion of esketamine could reduce the consumption of opioids at 24 and 48 hours postoperatively in patients undergoing gynecological laparoscopic surgery. The opioid-sparing effect of esketamine was not related to an increased risk of adverse events.

Despite the increasing types of medications and techniques available for postoperative pain management, a large proportion of surgical patients still experience significant postoperative pain.[20] It has been shown that opioid-sparing multi-modal analgesia strategies might reduce opioids requirement, decrease the incidence of adverse events, and facilitate postoperative recovery.[21–23] Esketamine, an NMDA receptor antagonist that also binds to μ-opioid receptors, increases concentrations of serotonin and norepinephrine in the brain,[24] so as to prevent nociceptive system activation and hyperalgesic effects of opioids.[25] This mechanism suggests that esketamine might be an ideal agent for multimodal analgesia. A previous study indicated that intravenous patient-controlled analgesia using hydroxyketone combined with esketamine might reduce opioid consumption following lumbar fusion surgery without increasing the incidence of side effects.[26] A meta-analysis showed that esketamine administered as an adjunct during general anesthesia reduced the intensity of acute postoperative pain.[27] These studies suggest that esketamine has significant opioid-sparing effects in managing acute postoperative pain, aligning with the findings of this study.

Our data showed that a lower dose of esketamine was comparably effective to high-dose esketamine in reducing postoperative opioid consumption. Yuan et al demonstrated that infusion of esketamine at 0.25 mg/Kg/h during thoracoscopic surgery resulted in reduced consumption of hydromorphone at 24 and 48 hours following surgery when compared to the control group. However, a lower dose of esketamine infusion at 0.15 mg/Kg/h did not show significant differences in postoperative hydromorphone consumption from the control group.[28] Based on previous data and our results, we hypothesize that esketamine might exert its opioid-sparing effect within a certain range of dosage. On the

contrary, another study indicated that in opioid-naïve adults, intraoperative intravenous administration of esketamine at a rate of either 0.12 mg/Kg/h or 0.6 mg/Kg/h did not reduce the consumption of hydrocodone within postoperative 48 hours in patients undergoing lumbar fusion surgery.[29] The discrepancies among research could be attributed to heterogeneity in study populations, including variations in surgical procedures, gender, anesthetic regimen and history of preoperative pain. For instance, in the study conducted by Brinck et al, preoperative neuropathic pain was more common in the control group, which could influence the analgesic effects of the medication. These insights suggest that further investigation is necessary to determine the therapeutic efficacy and opioid-sparing effects of esketamine across different types of surgical patients.[26]

Furthermore, our study indicated that the occurrence of opioid-related adverse events, as well as psychotomimetic adverse events were comparable between the esketamine groups and the control group. Our results were consistent with a meta-analysis studying the influence of esketamine on acute pain after abdominal surgery in adults.[30] In contrast, another study indicated that intraoperative use of esketamine reduced the incidence of PONV after thoracoscopic lung resection (15% in the esketamine group vs 31.7% in the control group).[31] Since all patients in the three groups received two different antiemetics to prevent PONV, we speculate that this might be a reason for the lack of differences among our study groups. Additionally, the relatively small sample size of our study made it difficult to detect the differences between the three groups in the rates of opioid-related adverse effects like PONV, and esketamine-related psychotomimetic adverse events as well.

Our study had several limitations. Firstly, it was a single-center trial, and the generalizability of our conclusion needs to be verified across a broader patient population. Secondly, sample size of the present trial was determined based on the postoperative 24 hours PCA opioid consumption. Although our sample was sufficient to detect differences in opioid requirements, it was inadequate in detecting potential adverse effects or complications. Lastly, although our research highlighted the potential impact of esketamine in reducing postoperative opioid use, postoperative pain management is a complex, multifactorial issue. The effectiveness of pain management is influenced not only by pharmacological interventions but also by factors such as the patient's emotional state, psychological expectations, and individual biological differences. Thus, future research should consider the interactions between these variables to optimize esketamine's efficacy and satisfy patients' varied needs.

Conclusion

In summary, our study shows that the use of two different dosages of esketamine during gynecological laparoscopic surgery resulted in a comparable reduction in opioids consumption at 24 and 48 hours postoperatively, without increasing the risk of associated adverse events.

Data Sharing Statement

The data collected during the study are available from the corresponding author (Juying Jin) upon request. We intend to share the raw data and detailed research protocol. The data will be made available to the public within 12 months following the publication of the article and will be retained for at least 5 years for use by the research community.

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Disclosure

The authors report no conflict of interest.

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