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CLINICAL TRIAL REPORT

Preoperative Anxiety's Impact on the Median Effective Dose of Esketamine for Alleviating Propofol Injection Pain in Patients Undergoing Painless abortion: A Randomized, Double-Blind, Controlled Trial

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Background: Propofol injection pain (PIP) is a frequent adverse effect during anesthesia induction, impacting patient comfort and satisfaction. Esketamine has been shown to alleviate PIP, but the optimal dose, especially in relation to preoperative anxiety levels, remains unclear. Preoperative anxiety may heighten pain perception and influence analgesic requirements.

Methods: A randomized, double-blind, controlled trial was conducted at The Affiliated Women and Children's Hospital of Ningbo University. A total of 150 eligible patients scheduled for painless abortion were assessed using the Spielberger State Anxiety Inventory - State form (STAI-S) and categorized into non-anxious (STAI-S score <40) and anxious (STAI-S score ≥40) groups. Patients were randomized using a computer-generated random number table to receive one of five escalating doses of esketamine (0.10, 0.12, 0.14, 0.17, or 0.20 mg/kg) prior to propofol administration. The primary outcome was the occurrence of PIP, assessed using Ambesh's four-point pain scale. Secondary outcomes included hemodynamic parameters and adverse events such as hypotension, bradycardia, and hypoxemia.

Results: A clear dose-response relationship was observed, with higher doses of esketamine significantly reducing the incidence of PIP in both groups. Anxious patients required higher doses of esketamine to achieve comparable pain relief to non-anxious patients. The effective dose for 50% of patients (ED_{50}) in the non-anxious group was 0.114 mg/kg (95% CI: 0.096–0.129 mg/kg), whereas it was 0.133 mg/kg (95% CI: 0.117–0.146 mg/kg) in the anxious group, with the difference being statistically significant ($P < 0.05$). No significant differences were observed between groups in terms of adverse events or hemodynamic stability.

Conclusion: Preoperative anxiety significantly increases the ED_{50} of esketamine required to alleviate propofol injection pain in patients undergoing painless abortion. Anxious patients require higher doses of esketamine to achieve effective analgesia. Individualizing esketamine dosing based on preoperative anxiety levels may enhance patient comfort and optimize pain management during anesthesia.

Keywords: propofol injection pain, esketamine, preoperative anxiety, painless abortion, anesthesia, dose-response

Introduction

Painless abortion is a form of induced abortion performed under anesthesia, which has the advantages of reducing pain and fear, and has become a core component of modern comfortable medical care.[1] Propofol is the most commonly utilized intravenous anesthetic in painless diagnosis and treatment due to its quick onset, brief action duration, minimal

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accumulation risk, and limited side effects. The frequency of Propofol injection pain (PIP) can reach up to 94%,[1] ranking it as the 7th significant issue in anesthesia practice. To lower the occurrence of PIP, different methods have been developed, such as modifying the temperature[2] or concentration of Propofol,[3] choosing larger veins,[4,5] and using percutaneous acupoint electrical stimulation.[6] However, the most commonly used method is still drug pretreatment, such as lidocaine,[2,6,7] nonsteroidal anti-inflammatory drugs,[8] dexmedetomidine,[2] ketamine,[7] opioid drugs.[7] Although various techniques or drugs have achieved certain effectiveness in relieving PIP, problems such as pulmonary embolism, gastrointestinal ulcers, prolonged anesthesia time, and agitation during the recovery period have restricted their widespread clinical application,[9] so the complete elimination of PIP has not yet been achieved.

Esketamine, as a new form of right-handed ketamine, has an anesthetic effect equivalent to twice that of racemic ketamine and approximately four times that of left-handed ketamine. Esketamine exhibits a more potent pain-relieving effect and faster elimination from the body compared to ketamine, requiring only half the dosage.[10,11] Prior research has demonstrated that administering a small amount of esketamine can successfully decrease the occurrence of injection discomfort in individuals undergoing general anesthesia.[10] However, the exact dose of esketamine for preventing injection pain is not yet clear.

Preoperative anxiety, characterized feelings of unease, tension, and fear before surgery, is a psychological response to perceived challenges or threats in reality. Literature reports indicate that about 60–70% of patients exhibit symptoms of anxiety before surgery,[12] with a higher proportion among female patients.[13] Patients undergoing general anesthesia and those who are generally prone to anxiety are more likely to experience anxiety before surgery. Additionally, studies have confirmed that preoperative anxiety is an independent risk factor for propofol injection pain.[14] This anxiety triggers activation of the sympathetic nervous system, resulting in physiological responses such as increased heart rate, elevated blood pressure, and enhanced pain sensitivity, which in turn may intensify the perception of pain during procedures.[15]

Consequently, A randomized, double-blind, controlled study was conducted to examine the impact of varying levels of preoperative anxiety on the esketamine dosage required to alleviate PIP in patients undergoing painless abortion. The primary objective was to determine the influence of anxiety on the median effective dose (ED_{50}) of esketamine for PIP relief, while secondary objectives included evaluating esketamine's safety profile, hemodynamic stability, and adverse events. The research hypothesis posited that higher anxiety levels increase the required esketamine dose for effective analgesia.

Methods

Design

Approval for the study was granted by the Ethics Committee at The Affiliated Women and Children's Hospital of Ningbo University, China (No.EC2021-031). The study adhered to the Consolidated Standards of Reporting Trials guidelines and complied with the Declaration of Helsinki. It was subsequently registered at http://www.chictr.org.cn with the identifier ChiCTR2200060873, led by principal investigator Yanping. Shen; date of registration: June 13, 2022). Every individual provided informed consent in writing.

Subjects and Setting

Our intention was to enroll 150 painless abortion participants at The Affiliated Women and Children's Hospital of Ningbo University. Participants were required to meet specific criteria, including ASA physical status I–II, being between the ages of 20–40, having a BMI of 19–26 kg/m^2, and having a Mallampati grade of I–II. Exclusion criteria were as follows: individuals with hypertension, high intraocular pressure, or high intracranial pressure; those with neurological or psychiatric disorders who were unable to communicate; a history of hyperthyroidism; individuals with allergies to esketamine or propofol; and those who had not received treatment with anti-anxiety, anti-depression, or opioid drugs before treatment.

While in the waiting area, every patient was instructed to fill out the Spielberger State Anxiety Inventory (STAI) survey. The STAI-S (State Anxiety) is comprised of 20 questions utilizing a 4-point Likert scale to inquire about participants' present emotions. Scores can range from 20 to 80, with higher scores indicating greater levels of anxiety. Scores below 40 are considered non-anxious, while scores equal to or above 40 are classified as anxious.[16]

Patients were stratified into two groups: group N comprised 75 non-anxious individuals, while group A consisted of 75 anxious individuals. IBM SPSS Statistics for Windows V.25.0 (IBM) was used to create a table of random numbers. Based on this table, each group's participants were then randomly assigned to five equally sized subgroups (15 participants per group). After dividing into subgroups, each was assigned randomly to receive one of five different amounts of esketamine: 0.10, 0.12, 0.14, 0.17, or 0.20 mg/kg, with consecutive doses increasing by a ratio of 1:1.2. In order to maintain blinding, 150 sealed opaque envelopes with sequential numbers were used to safeguard the drug allocation information and were opened prior to the propofol injection. The randomization process and drug preparation were conducted by a researcher (SYP) who was not involved in data collection or patient management. Dosing schedules were established using our previously documented explanations and practical knowledge. The doses were combined with saline solution to reach a 5 mL volume for the purpose of blinding.

Study Protocol

Prior to surgical procedures, participants were instructed to undergo an 8-hour fasting period and refrain from fluid intake for 2 hours, with no premedication administered. Upon entering the operating room, standard monitoring procedures were put in place to evaluate heart rate (HR), non-invasive blood pressure (NIBP), and pulse oximetry (SpO2), along with providing oxygen at a rate of 3 L/min through a nasal cannula. The anesthesiologist used a 20 gauge catheter to insert into the vein on the back of the left hand, allowing for the quick administration of sodium lactate Ringer's solution at a rate of 5 milliliters per kilogram. Subsequent to grouping, esketamine 5mL (lot number: 210421BL, manufactured by Jiangsu Hengrui Pharmaceuticals Co., Ltd.) was administered in varying doses, followed, after a 60-second interval, by a meticulously controlled intravenous infusion of 1% propofol at a dosage of 2 mg/kg (lot number: 5A210502, manufactured by Guangdong Jiabo Pharmaceutical Co., Ltd.) at an infusion rate of 0.4 mL/s. Throughout the administration process, an experienced anesthesiologist (YLJ) continuously engaged with the patient to assess for any discomfort in the limb and meticulously observed for verbal responses, facial expressions, and limb movements, such as retraction attempts. Anesthesia management for non-painful abortion was consistently overseen by the same anesthesiologist (HYL), with all surgical procedures performed by a singular senior gynecologist. In instances of patient movement during the procedure, an intravenous bolus of propofol (20 to 50 mg) was administered to enhance anesthesia depth. If respiratory depression happens (when the patient's breathing rate is less than 10 breaths/min or SpO2 is below 90%), the anesthesiologist in charge will first try to lift the patient's jaw manually, and if that does not work, they will increase oxygen supply using a pressurized mask. For episodes of hemodynamic instability, appropriate vasoactive medications were administered, including a single intravenous dose of 50 μg/mL norepinephrine or 10 μg /mL epinephrine as necessary.

Measurement

The principal outcome assessed was the occurrence of PIP. The severity of this pain was categorized according to Ambesh's four-tier scale, where a score of 0 indicates absence of pain; 1 signifies mild pain, characterized by minor moaning or distressed facial expressions without any physical movement; 2 denotes moderate pain, evidenced by noticeable moaning accompanied by physical movement; and 3 reflects severe pain, characterized by vocal complaints of intense pain, distressed facial expressions, withdrawal of the arm, or crying. Pain associated with injection was classified as negative for scores between 0 and 1, and positive for scores ranging from 2 to 3.

Data were systematically recorded at several predefined intervals: T1 (before the administration of any medication), T2 (after Propofol injection), and T3 (at the end of the surgical procedure). The measurements included systolic and diastolic blood pressure, oxygen saturation measured by pulse oximetry, and heart rate. Intraoperative hypoxemia (SpO2 below 90%), hypotension (more than 20% decrease from initial blood pressure or SBP below 90 mm Hg), and notable heart rate fluctuations (variation over 20% from baseline) were observed. The Ramsay scale was used to assess sedation levels during the postoperative recovery phase, with a score of 1 indicating emergence agitation. Adverse effects like queasiness, throwing up, confusion, and vision problems were carefully documented as well.

Statistical Considerations

Based on initial trial data, the sample size was determined for five increasing doses of esketamine: 0.10mg/kg, 0.12mg/kg, 0.14mg/kg, 0.17mg/kg, and 0.20mg/kg, resulting in Propofol injection pain(PIP) incidences of 70%, 60%, 50%, 30%, and 10%, respectively. The calculation of sample size was performed using the Cochran-Armitage Test for Trend in proportions method, which can be found in PASS15 software developed by NCSS, LLC in Kaysville, UT. The examination utilized a Z-test with continuity correction, with a significance level of 0.05 and statistical power of 0.90, necessitating the enrollment of 11 participants in each group. In order to reduce the confidence interval (CI) even more, the number of patients in each group was raised to 15.

Demographic information was displayed as either mean ± standard deviation (SD) or median (interquartile range) based on the distribution. The Kolmogorov–Smirnov test was employed to assess the normality of data distribution. Normally distributed quantitative data were analyzed using the independent samples *t*-test, whereas non-normally distributed quantitative data were assessed with the Mann–Whitney *U*-test. The frequency data was examined using either the Chi-square test or Fisher's exact test, depending on the circumstances.

The dose-response relationship for esketamine was established through probit regression analysis as previously described. The effective dose for 50% of patients (ED_{50}) and the effective dose for 95% of patients (ED_{95}) were determined for each group with 95% confidence intervals (CIs). To confirm differences in ED_{50} values between groups, the relative median potency (ratios of ED_{50}) was calculated. Statistical analyses were performed using SPSS V.26.0 and Microsoft Excel 2010.A *P*-value below 0.05 was deemed to be statistically significant.

Results

Between January 2023 and August 2023, a total of 162 individuals were evaluated for qualification. The enrollment of participants can be seen in Figure 1. The demographic data are shown in Table 1. There were no significant differences in age, weight, BMI, ASA classification, Mallampati grade, and duration of surgery between the two groups ($P>0.05$).

Table 2 shows the incidence of PIP in both groups at different doses of esketamine. It was observed that as the dose of esketamine increased, the incidence of positive PIP responses decreased in both groups. However, there was no statistically significant difference in the incidence of positive PIP between the two groups at any given dose ($P > 0.05$).

Figure 2 depicts the dose-response curves of esketamine in two groups. The R^2 coefficients for the probit regression lines for each group of patients were 0.965 and 0.994, demonstrating a strong alignment between the model and the data. The ED_{95} and ED_{50} values (95% confidence interval) of esketamine for relieving PIP in non-anxiety patients were 0.184 (95% CI 0.165–0.215) and 0.114 (95% CI 0.096–0.129) mg / kg, respectively. The ED_{95} and ED_{50} values of esketamine in relieving PIP in anxiety patients were 0.202 (95% CI 0.182–0.238) mg/kg and 0.133 (95% CI 0.117–0.146), respectively. A notable contrast was observed between the two groups, with an ED_{50} ratio of 0.018 (95% CI 0.001 to 0.045).

At time point T1, Group N showed significantly higher SBP, DBP, and HR than Group A ($P < 0.05$), as shown in Figure 3. Nevertheless, there were no variances in systolic blood pressure, diastolic blood pressure, and heart rate among the two groups at both time points T2 and T3. Group N did not show any variations in SBP, DBP, and HR across different time intervals. However, the anxiety group exhibited a notable reduction in SBP, DBP, and HR at T2 and T3 in comparison to T1, demonstrating statistical significance.

Mild to moderate adverse events were observed, with no severe adverse events documented in Table 3. There were no statistically significant differences between the two groups in the incidence rates of hypotension, bradycardia, hypoxemia, jaw thrust, nausea/vomiting, or motor response ($P> 0.05$). Delirium was not observed in any of the patients from either group.

Discussion

The study aimed to assess how preoperative anxiety affects the ED_{50} of esketamine for PIP in patients undergoing painless induced abortion. According to our research findings, the anxiety state significantly affects the efficacy of

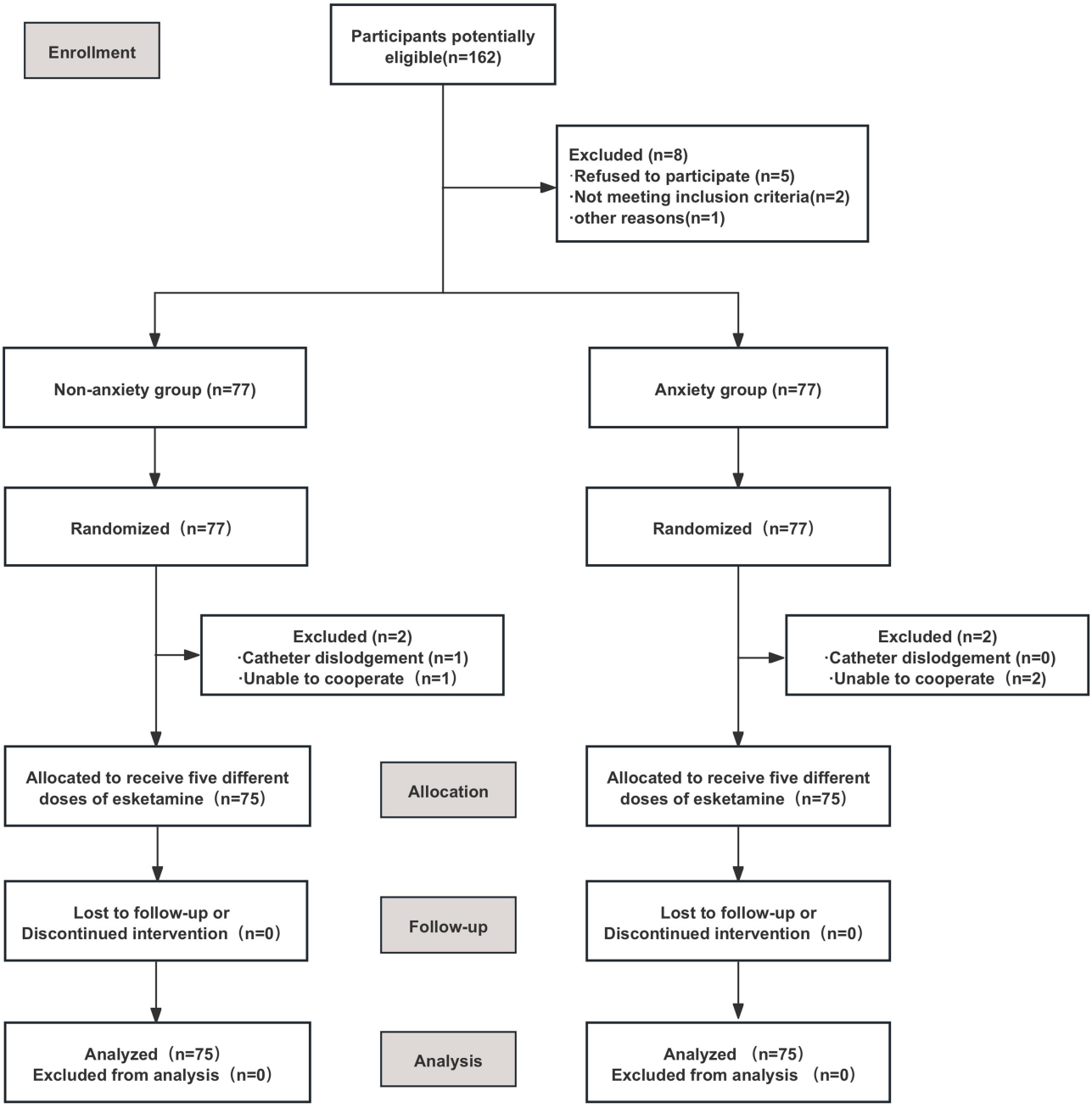

Figure 1 CONSORT chart illustrating the patient flow in the study's two groups. CONSORT stands for Consolidated Standards of Reporting Trials.

esketamine, resulting in anxious patients requiring higher doses of esketamine to achieve the same analgesic effect as non-anxious patients.

Propofol is frequently utilized as an intravenous anesthetic in painless induced abortion procedures because of its strong sedative-hypnotic properties. However, the incidence of injection pain is high, affecting patient comfort and experience. The mechanism of pain is unclear, with some suggesting that PIP has two basic mechanisms associated with propofol.[17] The phenol group in propofol stimulates the skin, mucous membranes, and vein walls, triggering pain receptors and nerve endings, leading to intimate sensations. Secondly, it activates endothelial cells indirectly by affecting propofol. It has been clinically observed that preoperative anxiety further affects PIP.

Table 1 Demographic Data

	Group N (n=75)	Group A (n=75)	P value*
Age (years)	30.87± 5.64	29.92± 6.34	0.335
Weight (kg)	55.89±5.62	56.27±5.95	0.693
BMI (kg/m^2)	21.87±2.17	21.44±3.25	0.347
ASA (I/II)	39/36	43/32	0.512
Mallampati Grade (I/II)	45/30	39/36	0.411
Duration of surgery (min)	7.55±1.46	7.67±1.33	0.600
Duration of anesthesia(min)	12.43±1.72	12.72±2.00	0.336
Propofol dosage(mg)	127.60±19.14	130.80±20.17	0.321

Notes: *Student's *t*-test used to compare means of normally distributed data; Mann–Whitney *U*-test used to compare means of nonnormally distributed data.
Abbreviation: BMI, body mass index.

Table 2 Comparison of PIP Incidence with Different Doses of Esketamine Between Two Groups

Esketamine dose	Group N (n=75)	Group A (n=75)	*P* value*
	Ambesh score (0/1/2/3)	Ambesh score (0/1/2/3)	
0.10mg/kg	3/2/9/1	1/2/10/2	0.682
0.12mg/kg	4/5/5/1	3/3/7/2	0.466
0.14mg/kg	8/3/3/1	5/4/5/1	0.700
0.17mg/kg	11/2/2/0	8/4/3/0	1.000
0.20mg/kg	13/2/0/0	11/3/1/0	1.000

Notes: *The P value represents the comparison of the number of positive PIP cases within the same dose of esketamine between the two groups.

Preoperative anxiety is often described as an unpleasant emotional state of anxiety, tension, and fear before surgery, reflecting an individual's emotional response to potential challenges or threats in reality.[13,14,18] Female patients generally exhibit higher levels of preoperative anxiety than male patients,[13] and patients undergoing general anesthesia surgery or

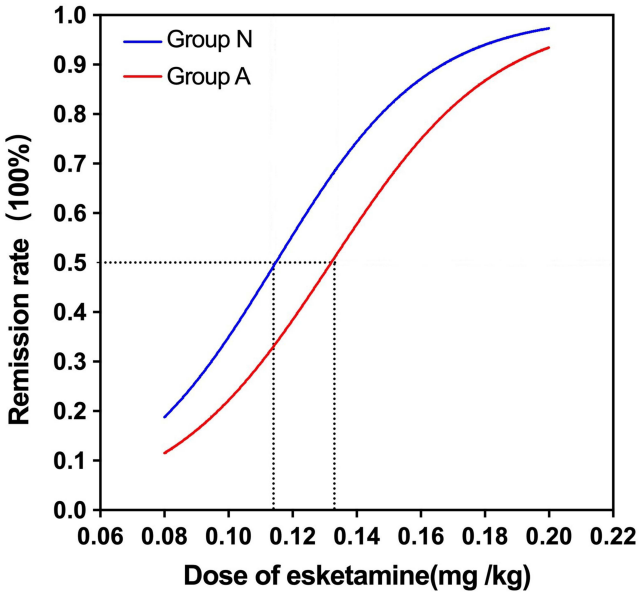

Figure 2 Probit regression was used to create dose-response curves for the pain caused by propofol injection in patients undergoing painless abortion. The curves were generated for non-anxious (Group N, blue curve) and anxious patients (Group A, red curve). The estimates of ED50 are shown with dashed lines.

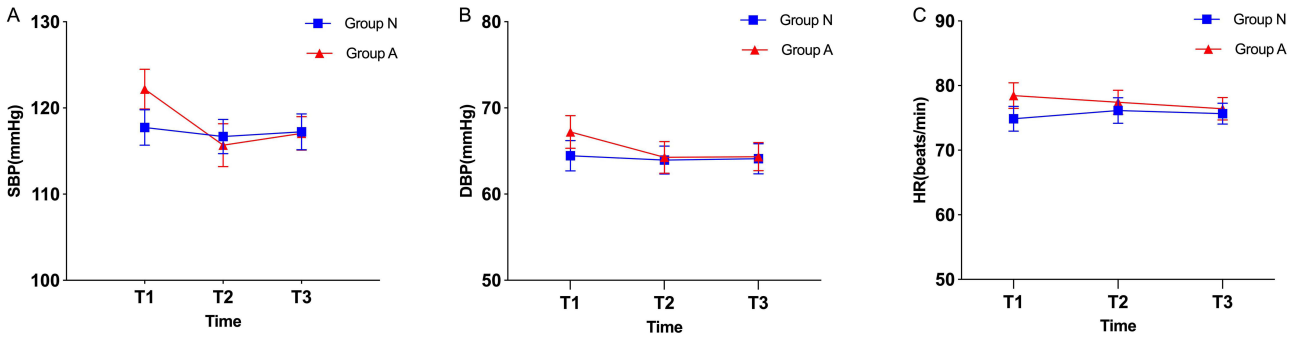

Figure 3 Changes of vital signs (**A–C**).
Notes: Data are displayed as Mean ± SD. Time points: T1, at the time before the administration of any medication; T2, after Propofol injection; T3, at the end of the surgical procedure.
Abbreviations: SBP, systolic blood pressure; DBP, diastolic blood pressure; HR, heart rate.

those who are prone to anxiety are more likely to experience preoperative anxiety. Therefore, we chose painless induced abortion patients. Preoperative anxiety may enhance the perception of propofol injection pain through several mechanisms. Firstly, anxiety can increase the patient's anticipation of pain, thereby enhancing pain sensitivity. Psychological theories such as pain amplification theory suggest that anxiety and fear can increase pain perception through central sensitization.[19] Additionally, anxiety can impact the patient's hormonal reaction, for example, by triggering the HPA axis to secrete cortisol, which can indirectly influence pain tolerance.[20] Ip et al stated that mental aspects play a bigger role in how pain is felt compared to physical factors, with anxiety raising and lowering the patient's sensitivity to pain. Psychological factors are believed to affect patient pain thresholds and postoperative pain sensitivity.[21] The study by Miniksar et al[14] was proposed that high levels of anxiety before surgery can strongly indicate the likelihood of postoperative pain, with preoperative anxiety, type D personality, and pain from venous intubation being identified as separate risk factors for postoperative pain. A strong linear relationship exists between preoperative anxiety, sensitivity to pain, and the need for anesthesia, allowing for the prediction of anesthetic usage in individual patients.[18] Therefore, it is necessary to distinguish anxious patients to better guide clinical drug use. The STAI is a widely utilized tool for assessing anxiety levels globally. It is a self-administered questionnaire that mainly reflects the subject's short-term tension and anxiety, especially suitable for measuring anxiety levels in acute stress situations such as surgical stress. The higher the score obtained by the subject, the higher their level of anxiety. In this study, a score of 40 was used as the cutoff point, dividing the subjects into anxiety and non-anxiety groups.[16]

The most commonly used drug in clinical practice to alleviate PIP is esketamine. Esketamine functions as a blocker of the N-methyl-D-aspartate (NMDA) receptor. At minimal levels, esketamine can induce calming and pain-relieving

Table 3 Incidence of Adverse Events Between Two Groups [n,(%)]

	Group N (n=75)	**Group A (n=75)**
Hypotension	3 (4)	4 (5)
Hypoxemia (SpO2<90%)	9 (12)	11 (15)
Chin lift (SpO2<90%)	6 (4)	7 (5)
Bradycardia (<50beats/min)	5 (7)	4 (5)
Nausea and vomiting	0 (0)	1 (1)
Delirium	0 (0)	0 (0)
Body movement response	2 (3)	3 (4)

Notes: The data is presented as the total number of cases along with the corresponding percentage. The frequency of adverse events was analyzed using chi-square tests or Fisher's exact test. There is no statistical significance between the two groups ($P>0.05$).

impacts similar to ketamine, requiring only half the dosage of ketamine.[9,10,22–26] Research has shown that administering ketamine before treatment decreases PIP by affecting NMDA receptors in endothelial cells, resulting in local anesthesia, decreased release of bradykinin, and relief of pain pathways, in addition to the central analgesic effects of ketamine.[27] Esketamine, the right-handed version of ketamine, acts as a non-competitive antagonist of NMDA receptors,[26] showing a stronger binding affinity and potency compared to racemic ketamine, while also having fewer side effects.[28] Research by Chaozhi Xu et al[9] indicated that as the dose of esketamine (4mg, 12mg, and 20mg) increased, the effectiveness of relieving propofol injection pain improved. According to reference,[29] the pH of the combination of propofol and ketamine is 5.84, whereas the pH of propofol by itself is 7.86. The study results support that changes in pH are a more important reason for reducing propofol injection pain than the peripheral effects of ketamine. However, the study by Chaozhi Xu et al[9] may require larger doses of esketamine because esketamine is mixed with 1% propofol and then continuously infused, and the esketamine may not have taken effect at the beginning of the infusion. Dixon's up-and-down technique was employed by Meiyun Tan et al to establish that the effective dose for 50% relief of propofol injection pain with esketamine is 0.143 (0.120, 0.162) mg/kg, while the effective dose for 95% relief is 0.176 (0.159, 0.320) mg/kg.[24] The ED_{50} of this study was slightly higher than ours. On the one hand, this study administered propofol injections 30 seconds after esketamine injection. On the other hand, this study classified pain responses into four levels based on the VRS score, with a VRS score of 0 in the effective group defined as negative pain response (-), and VRS scores of 1–3 in the ineffective group defined as positive pain response (+), while our study defined Ambesh scores of 0–1 as negative injection pain and Ambesh scores of 2–3 as positive injection pain. The study showed that esketamine administered intravenously had an onset time of 30 seconds. In this study, esketamine was injected intravenously 60 seconds before propofol injection, allowing sufficient contact time with NMDA receptors on endothelial cell membranes while ensuring central analgesic effects before propofol stimulation. Since esketamine was administered at a low dose of 0.1 to 0.2 mg/kg, most patients who experienced dizziness and drowsiness were still able to verbally communicate and complete the Ambesh score assessment 60 seconds after the infusion. However, two patients in each group fell asleep and were subsequently excluded from the trial.

Esketamine has sympathomimetic effects, which are beneficial for maintaining hemodynamic stability in perioperative patients. In a study of elderly patients undergoing painless gastroscopy, researchers discovered that esketamine led to a notable decrease in the median effective concentration of propofol, along with a reduced occurrence of hypotension and quicker recovery time.[23] Administering low-dose esketamine to elderly patients undergoing knee arthroplasty can help stabilize hemodynamics, decreasing surgical risks and enhancing patient safety.[25] The research revealed that patients with preoperative anxiety exhibited notably elevated SBP, DBP, and HR compared to those without anxiety ($P<0.05$), potentially as a result of physiological stress reactions triggered by anxiety causing activation of the sympathetic nervous system, leading to increased blood pressure and heart rate. In intra-group comparisons, there were no significant differences at various time points in the non-anxiety group. In the anxiety group, there was a reduction after taking medication following surgery, but it did not show a notable contrast with the non-anxiety group. The incidence of hypotension was similar in both groups, indicating that esketamine potentially has an effect on stabilizing hemodynamics regardless of anxiety. A study examining painless oocyte retrieval found that patients with high anxiety levels needed more propofol to achieve sedation compared to those with low anxiety levels.[30] Many studies[31,32] have shown that an increase in anxiety levels is correlated with an increase in the dose of sedative drugs required. However, in this study, the doses of propofol used in both groups were similar, possibly due to the sympathomimetic activity of esketamine and its central analgesic effects offsetting the inhibitory effects of propofol.

Limitations of the Study

Although this research offers important information on how preoperative anxiety levels are connected to the effectiveness of esketamine in reducing postoperative pain in patients undergoing painless abortion, it is important to acknowledge the various constraints present. The study's limitation to a single center at The Affiliated Women and Children's Hospital of Ningbo University may hinder the generalizability of the findings to diverse clinical environments with varying patient characteristics and anesthesia protocols. Additionally, the strict exclusion criteria applied in this study and the sole reliance on the Spielberger State Anxiety Inventory (SAI) to assess preoperative anxiety may have limited the

representativeness of the study sample and the comprehensiveness of anxiety measurement. Furthermore, the use of Ambesh's four-tier scale for PIP assessment introduces subjectivity and may not fully capture pain intensity. To overcome these limitations, future studies should focus on using bigger and more varied samples, carrying out studies in multiple centers, including thorough anxiety assessment tools, using objective pain measurement techniques, and examining a wider range of outcome measures to gain a better understanding of the connection between anxiety, the effectiveness of esketamine, and relief from PIP.

Conclusion

To summarize, this study demonstrates that preoperative anxiety significantly influences the ED_{50} of esketamine required to alleviate PIP in patients undergoing painless abortion. Anxious patients required higher doses of esketamine (ED_{50} = 0.133 mg/kg) compared to non-anxious patients (ED_{50} = 0.114 mg/kg) to achieve similar analgesic effects. Esketamine was effective in reducing PIP with minimal adverse effects and maintained hemodynamic stability. These findings support the need for individualized esketamine dosing based on anxiety levels to improve patient comfort. Further multicenter studies are warranted to confirm these results and refine pain management strategies.

Data Sharing Statement

The data generated during the study can be obtained from the corresponding author (Liangguang Zhang) upon reasonable request.

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Disclosure

The authors declare that there is no conflict of interest.

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