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CLINICAL TRIAL REPORT

Efficacy of Different Doses of Remimazolam Tosilate Combined with Esketamine in Painless Abortion Patients: A Prospective, Double-Blind, Randomized Controlled Trial

Jiejuan Chen[1,*], Jingchao Zhang[2,*], Mazhong Zhang[1–3], Xiaohua Zou[4], Bailong Hu[4], Yang Yang[4], Hui Li[4]

[1]Department of Anesthesiology, Guizhou Medical University, Guiyang City, Guizhou Province, People's Republic of China; [2]Department of Anesthesiology, Guizhou Provincial People's Hospital, Guiyang City, Guizhou Province, People's Republic of China; [3]Department of Anesthesiology, Shanghai Children's Medical Center, School of Medicine, Shanghai Jiao Tong University, Shanghai, People's Republic of China; [4]Department of Anesthesiology, Affiliated Hospital of Guizhou Medical University, Guiyang City, Guizhou Province, People's Republic of China

*These authors contributed equally to this work

Correspondence: Mazhong Zhang; Xiaohua Zou, Email zmzscmc@shsmu.edu.cn; zouxiaohuazxh@163.com

Background: Remimazolam tosilate (RT) is a novel ultra-short-acting benzodiazepine with rapid onset, short half-life, stable hemodynamics, and minimal respiratory depression. This study aimed to assess the efficacy, safety, and optimal dosage of RT combined with esketamine for painless abortion procedures.

Methods: This single-center, prospective, randomized, double-blind trial was conducted from December 2022 to December 2024. A total of 210 patients (aged 18–45 years, ASA I–II, BMI 18–28 kg/m^2) undergoing elective painless abortion were randomly assigned to one of three groups: propofol 2 mg/kg (Group P), RT 0.2 mg/kg (Group RL), or RT 0.3 mg/kg (Group RH). Primary outcomes were perioperative hemodynamic changes, assessed by mean arterial pressure fluctuation value (ΔMAP) and heart rate fluctuation value (ΔHR). Secondary outcomes included adverse events, vital sign changes, induction and recovery times, surgical duration, time to discharge readiness, need for additional sedation, visual analogue scale (VAS) pain scores at awakening and discharge, and satisfaction levels of patients, surgeons, and anesthesiologists.

Results: The ΔMAP in Group RL (7.11 ± 2.49) was significantly lower than in Group P (11.93 ± 2.09) and Group RH (12.80 ± 2.59) ($F = 114.286$, $P < 0.001$), indicating more stable perioperative hemodynamics. Group RL also showed shorter recovery time and quicker discharge readiness. Hypotension incidence was lower in Groups P and RL compared to RH. Rates of hypoxemia, nausea/vomiting, and neuropsychiatric symptoms were significantly lower in Groups RL and RH than in Group P. RT required fewer supplemental doses than propofol, and patient satisfaction was highest in Group RL. No significant differences were observed among groups for ΔHR, induction time, surgical duration, hypertension, body movement, injection pain, postoperative pain, or patient/surgeon/anesthesiologist satisfaction.

Conclusion: Low-dose RT (0.2 mg/kg) combined with esketamine significantly shortens recovery and discharge times, ensures hemodynamic stability, and reduces adverse events, making it the recommended sedation strategy for painless abortion procedures.

Keywords: remimazolam tosilate, esketamine, propofol, painless abortion, hemodynamics

Introduction

In China, abortion is not legally restricted. As a common gynecological procedure, both the short- and long-term physiological and psychological effects of abortion are clinically significant. Consequently, optimizing painless and comfortable management remains a key focus in clinical anesthesia research.[1,2] Propofol has long been widely used in outpatient surgical anesthesia due to its rapid onset and quick recovery.[3,4] However, it is associated with hemodynamic

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instability,[5,6] respiratory depression,[7] and injection pain,[8,9] which may compromise patients' perioperative safety and comfort.[10]

Our preliminary studies found that combining esketamine, a highly selective NMDA receptor antagonist, with propofol for painless abortion reduced the required propofol dose, relatively stabilized hemodynamics, and alleviated injection pain, outperforming traditional combinations such as opioids with propofol. Furthermore, an optimal esketamine dose of 0.25 mg/kg for painless abortion was preliminarily established.[11] However, adverse effects associated with propofol, particularly respiratory and circulatory depression, remain significant, highlighting the need for safer alternatives.

Remimazolam tosilate (RT), a novel ultra-short-acting benzodiazepine, has emerged as a promising agent for ambulatory anesthesia due to its short half-life, organ-independent metabolism, hemodynamic stability, and minimal respiratory depression.[12,13] Studies have shown that RT produces rapid sedation by enhancing $GABA_A$ receptor-mediated inhibitory neurotransmission, without significantly affecting vascular smooth muscle, thereby minimizing blood pressure fluctuations.[14] Notably, RT alone lacks analgesic properties and must be combined with an analgesic to meet surgical requirements. Esketamine, with its potent analgesic effects, serves as an ideal complement.[15]

Research has demonstrated that the combination of RT and esketamine exerts a synergistic effect in short-duration procedures such as painless gastrointestinal endoscopy. Compared with esketamine alone, this combination improves intraoperative hemodynamic stability, shortens recovery time, and reduces the incidence of respiratory depression.[16,17]

However, systematic research on the synergistic effects, dose–response relationship, and safety profile of RT combined with esketamine remains lacking. Therefore, this study aims to conduct the first comprehensive evaluation of the efficacy and safety of RT combined with esketamine for painless abortion through a prospective randomized controlled trial. It also seeks to determine the optimal RT dosage, thereby providing evidence to support improved anesthesia protocols for ambulatory surgery and advancing safer, more comfortable painless abortion management strategies. Additionally, while this study is conducted in China, its findings may have global relevance for broader clinical applications, as the challenges of optimizing anesthesia safety and efficacy in outpatient settings are universal, and similar approaches could be adapted to other healthcare systems worldwide.

Methods

This study was a prospective, randomized, double-blind, single-center trial designed to evaluate the efficacy and safety of different doses of RT combined with esketamine in patients undergoing elective artificial abortion. The protocol was approved by the Ethics Committee of Guizhou Medical University (Ref: 2021163) and registered with the Chinese Clinical Trial Registry (ChiCTR2100047190, Registration date: June 10, 2021). The study was conducted in accordance with the Declaration of Helsinki. Written informed consent was obtained from all participants prior to enrollment. A flowchart outlining the study design is presented in Figure 1.

Eligibility Criteria

Patients aged 18–45 years, with American Society of Anesthesiologists (ASA) physical status I–II and a body mass index (BMI) between 18 and 28 kg/m^2, who were scheduled for outpatient painless abortion between June 2023 and December 2024, were eligible for inclusion. Exclusion criteria were as follows: (1) history of vaginal delivery; (2) hearing impairment; (3) significant preoperative respiratory or circulatory dysfunction, or abnormal routine blood or biochemical test results; (4) severe neuropsychiatric disorders; (5) infectious diseases; (6) regular use of benzodiazepines or opioids within the past month or intermittent use within the past three months; (7) known allergies or contraindications to opioids, propofol, or any of their components; (8) anticipated difficult airway, defined as a Modified Mallampati score of class III or higher; (9) participation in other ongoing clinical trials; and (10) any condition deemed by the investigator to make the patient unsuitable for the study.

Rationale for Key Eligibility Criteria

Specific eligibility criteria were implemented to ensure cohort homogeneity, control confounding variables, and safeguard participant welfare. Exclusion of parous women (history of vaginal delivery) controlled for potential confounding

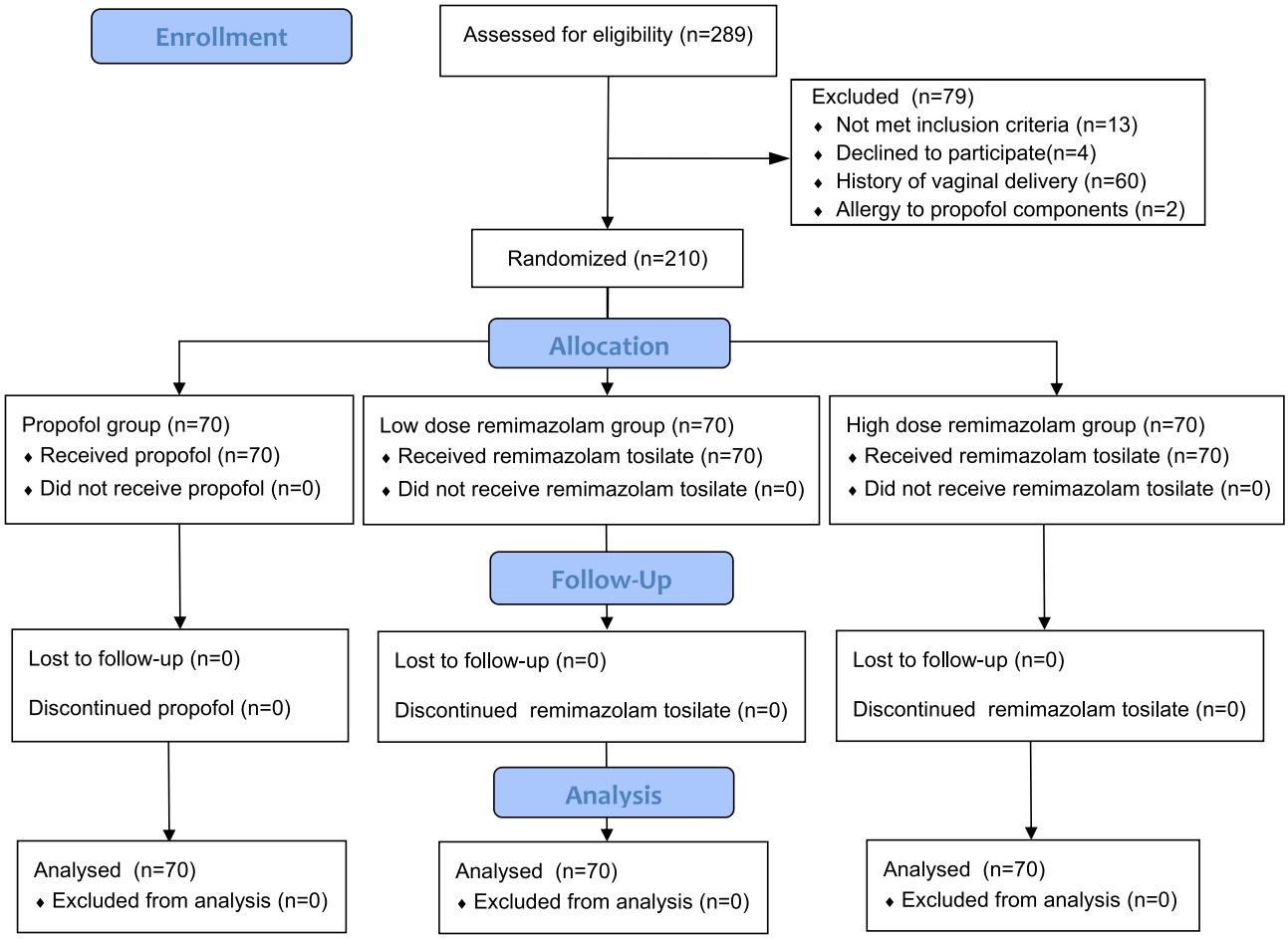

Figure 1 Consort flow diagram of the trial design.

from parity-induced differences in cervical compliance. Patients with hearing impairment were excluded to ensure the reliability of responsiveness assessments using the Modified Observer's Assessment of Alertness/Sedation (MOAA/S) scale. Recent use of benzodiazepines or opioids was prohibited to eliminate pharmacodynamic interactions. Restriction to ASA I–II and BMI 18–28 kg/m² minimized physiological variance related to comorbidities. Exclusion of patients with a Modified Mallampati score of class III or higher mitigated risks associated with difficult airway management during procedural sedation.

Randomization and Blinding

A randomization sequence was generated using a 1:1:1 allocation ratio by an anesthesiologist not involved in data collection or analysis. Randomization numbers were sealed in sequentially numbered, opaque envelopes, which were opened only after the patient entered the operating room. Based on the randomization results, patients were assigned to one of three groups: propofol 2 mg/kg group (Group P), low-dose RT 0.2 mg/kg group (Group RL), or high-dose RT 0.3 mg/kg group (Group RH).

An anesthesia assistant not involved in the trial prepared all syringes containing the study drugs and masked them with opaque tape to conceal drug identity. To maintain allocation concealment, data collection was carried out by a research physician blinded to group assignments, and statistical analysis was conducted by another physician who was also unaware of the group allocations. Throughout the study, patients, attending anesthesiologists, nurses, and investigators remained blinded to randomization and allocation details.

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Study Interventions

All patients were instructed to fast for 8 hours prior to surgery. Upon arrival in the operating room, standard monitoring was initiated, including electrocardiogram (ECG), noninvasive blood pressure (NIBP), and peripheral oxygen saturation (SpO_2) measurements. Oxygen was administered via a simple face mask at 4–6 L/min. Anesthesia induction began after 3 minutes of preoxygenation.

All patients received intravenous esketamine at a dose of 0.25 mg/kg, administered over 30 seconds. Following this, Group P received propofol 2 mg/kg, Group RL received RT 0.2 mg/kg, and Group RH received RT 0.3 mg/kg, each infused intravenously over approximately 30 seconds. Sedation depth was monitored using the Modified Observer's Assessment of Alertness/Sedation (MOAA/S) scale, assessed immediately after drug administration and then at 30-second intervals until a score of $\leq$2 was achieved. At this point, the surgical procedure commenced. The time from drug administration to reaching an MOAA/S score $\leq$2 was recorded.

The MOAA/S scale ranges from 0 to 5, with each level indicating a different degree of responsiveness. A score of 0 signifies no response to painful stimuli, while a score of 1 indicates a response only to painful stimuli, such as a trapezius squeeze. A score of 2 reflects a response to light touch or vibration, whereas a score of 3 corresponds to a response to loud or repeated name calling. A score of 4 denotes a delayed response to name calling in a normal tone, and a score of 5 represents a prompt response to name calling in a normal tone.

All patients maintained spontaneous respiration throughout the procedure. Additionally, adverse events were documented and managed accordingly. The following conditions were specifically defined and treated as follows: Hypotension, identified by a systolic arterial pressure of less than 80 mmHg or a decrease of more than 20% from baseline, was treated with 6 mg of intravenous ephedrine. Hypertension, defined as a mean arterial pressure (MAP) greater than 120 mmHg, was managed using an appropriate dose of nitroglycerin. Bradycardia, characterized by a heart rate (HR) below 50 bpm, was treated with 0.5 mg of intravenous atropine. Hypoxia, indicated by an SpO_2 level below 90%, was managed through assisted manual ventilation via a face mask. Somatic motor responses were addressed with an intravenous dose of propofol at 0.5 mg/kg. Nausea and vomiting were treated with 0.25 mg of intravenous palonosetron.

The total supplemental doses of propofol and RT, surgery duration, anesthesia induction time, recovery time (defined as the interval from the final drug dose to achieving a MOAA/S score $\geq$4), and time to meet discharge criteria were recorded. Postoperative pain was assessed using the visual analog scale (VAS) at both awakening and discharge, along with documentation of injection pain.

Discharge readiness was evaluated by the investigator 10 minutes after the procedure and every 5 minutes thereafter until the patient met all criteria for safe discharge with a family member. Discharge criteria included: blood pressure and HR within ±20% of baseline and stable for $\geq$10 minutes; no or only mild pain; no or only mild nausea/vomiting; no dizziness while sitting or walking; and the ability to walk independently at least 2 meters in a straight line after removal of monitoring equipment.

After full recovery and once patients were fully alert, they rated their satisfaction with the procedure and reported any intra-procedural discomfort or undesirable experiences. The operating surgeon and anesthesiologist also independently rated their satisfaction with the anesthetic management.

Assessment of Primary and Secondary Outcomes

The primary outcome of this study was the change in hemodynamic parameters, specifically ΔMAP and ΔHR. ΔMAP was defined as the difference between the highest or lowest MAP and the baseline MAP. Similarly, ΔHR was defined as the difference between the highest or lowest HR and the baseline HR. Secondary outcomes included perioperative vital signs at specified time points, the incidence of adverse events, duration of surgery, anesthesia induction time, recovery time, time to meet discharge criteria, the number of supplemental doses of propofol or RT required, postoperative pain scores, as well as patient, surgeon, and anesthesiologist satisfaction levels across the three groups.

Data Analysis

The study aimed to enroll 210 participants in a randomized controlled trial designed to compare the effects of RT and propofol on hemodynamic parameters in patients undergoing painless abortion, while also exploring the optimal RT dosage. Participants were randomly assigned to one of three groups: propofol 2 mg/kg (Group P), low-dose RT 0.2 mg/kg (Group RL), or high-dose RT 0.3 mg/kg (Group RH).

The sample size calculation was based on the primary outcome measure: changes in hemodynamic parameters (ΔMAP). Preliminary data from 10 patients in each group indicated mean ΔMAP values of 12.02 ± 3.05 mmHg in Group P, 10.37 ± 3.19 mmHg in Group RL, and 13.11 ± 4.03 mmHg in Group RH. Assuming $\alpha = 0.05$ and power = 0.90, the required sample size was calculated using one-way analysis of variance (ANOVA) with Tukey's post hoc test in PASS 15 software (NCSS, LCC, Kaysville, UT, United States). The estimated total sample size was 168 patients (56 per group). A total of 210 patients were enrolled in this study (n = 65 in each group) to account for a potential withdrawal rate of 20%.

Data analysis was conducted using SPSS version 25.0 (IBM Corp., Armonk, NY, USA). Continuous variables were expressed as mean ± standard deviation () for normally distributed data or median (interquartile range) [M (IQR)] for skewed data. Categorical variables were reported as frequency and percentage [n (%)]. Normality was assessed using the Shapiro–Wilk test. For comparisons among three groups: Normally distributed data were analyzed using one-way ANOVA or repeated-measures ANOVA for time-dependent variables, followed by Tukey's post hoc test for one-way ANOVA or Bonferroni-adjusted pairwise comparisons for repeated measures. Non-normally distributed data were analyzed using the Kruskal–Wallis test, with Dunn's post hoc test. Categorical variables were compared using the chi-square test or Fisher's exact test, as appropriate. All statistical tests were two-sided, and a p-value < 0.05 was considered statistically significant.

Results

A total of 289 patients were screened for this study. Thirteen failed to meet inclusion criteria, four declined participation, sixty had previous vaginal delivery histories, and two were allergic to propofol components. Consequently, 210 patients were randomized and included in the final analysis (Figure 1). All screening occurred prior to group allocation. Baseline characteristics and demographic data for the three groups are summarized in Table 1. There were no statistically significant differences among the groups in terms of age, height, weight, BMI, ASA classification, or the number of patients undergoing first-trimester abortion.

The MAP fluctuation (ΔMAP) in the RL group was significantly lower than that in both Group P and the RH group (ΔMAP: RL group 7.11 ± 2.49, Group P 11.93 ± 2.09, RH group 12.80 ± 2.59; $F = 114.286$, $P < 0.001$). However, no statistically significant difference in ΔMAP was observed between Group P and the RH group. Additionally, there were no significant differences in ΔHR among the three groups (Table 2).

The RL group exhibited significantly higher MAP values than both Group P and the RH group when MOAA/S ≤ 2 and at the end of surgery, and significantly higher MAP values than the RH group at awakening ($P < 0.05$). At surgery

Table 1 Demographic and Baseline Characteristics of Patients

Variable	Group P (n=70)	Group RL (n=70)	Group RH (n=70)	F/χ^2	*P*-value
Age (years)	30.51 ± 5.59	28.97 ± 5.91	28.90 ± 5.95	1.720	0.182
Height (cm)	157.63 ± 4.79	158.66 ± 4.77	158.57 ± 4.62	1.020	0.363
Weight (kg)	53.11 ± 7.80	54.10 ± 5.97	53.72 ± 6.12	0.394	0.675
BMI (kg/m^2)	21.48 ± 2.57	21.52 ± 2.32	21.38 ± 2.23	0.058	0.944
ASA (I/II)	56/14	58/12	55/15	0.424	0.862
Number of first pregnancy abortions, yes/no	23/47	26/44	25/45	0.292	0.903

Notes: Variables presented as mean ± SD and number of patients. F-test, Chi-square test and Fisher' s exact test were used for data analysis.
Abbreviations: Group P, 2 mg/kg propofol group; Group RL, 0.2 mg/kg remimazolam group; Group RH, 0.3 mg/kg remimazolam group; BMI, body mass index; ASA, American Society of Anaesthesiologists.

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Table 2 Haemodynamic Fluctuations Between the Three Groups

Variable	Group P (n=70)	Group RL (n=70)	Group RH (n=70)	F	*P*-value
ΔMAP	11.93 ± 2.09	7.11 ± 2.49	12.80 ± 2.59	114.286	<0.001*
ΔHR	6.87 ± 2.10	6.60 ± 2.36	7.26 ± 2.30	1.499	0.226

Notes: Variables presented as mean ± SD. *$P < 0.05$ vs Group RL, F-test and Bonferroni method were used for data analysis. *P*-value is the Bonferroni correction value.
Abbreviations: Group P, 2 mg/kg propofol group; Group RL, 0.2 mg/kg remimazolam group; Group RH, 0.3 mg/kg remimazolam group; ΔMAP, mean arterial pressure fluctuation value; ΔHR, heart rate fluctuation value.

initiation, and 1 and 3 minutes after surgery began, both the RL group and Group P showed significantly higher MAP values than the RH group ($P < 0.001$). No significant differences were observed in HR, SpO_2, or MOAA/S scores among the three groups at any time point (Figure 2).

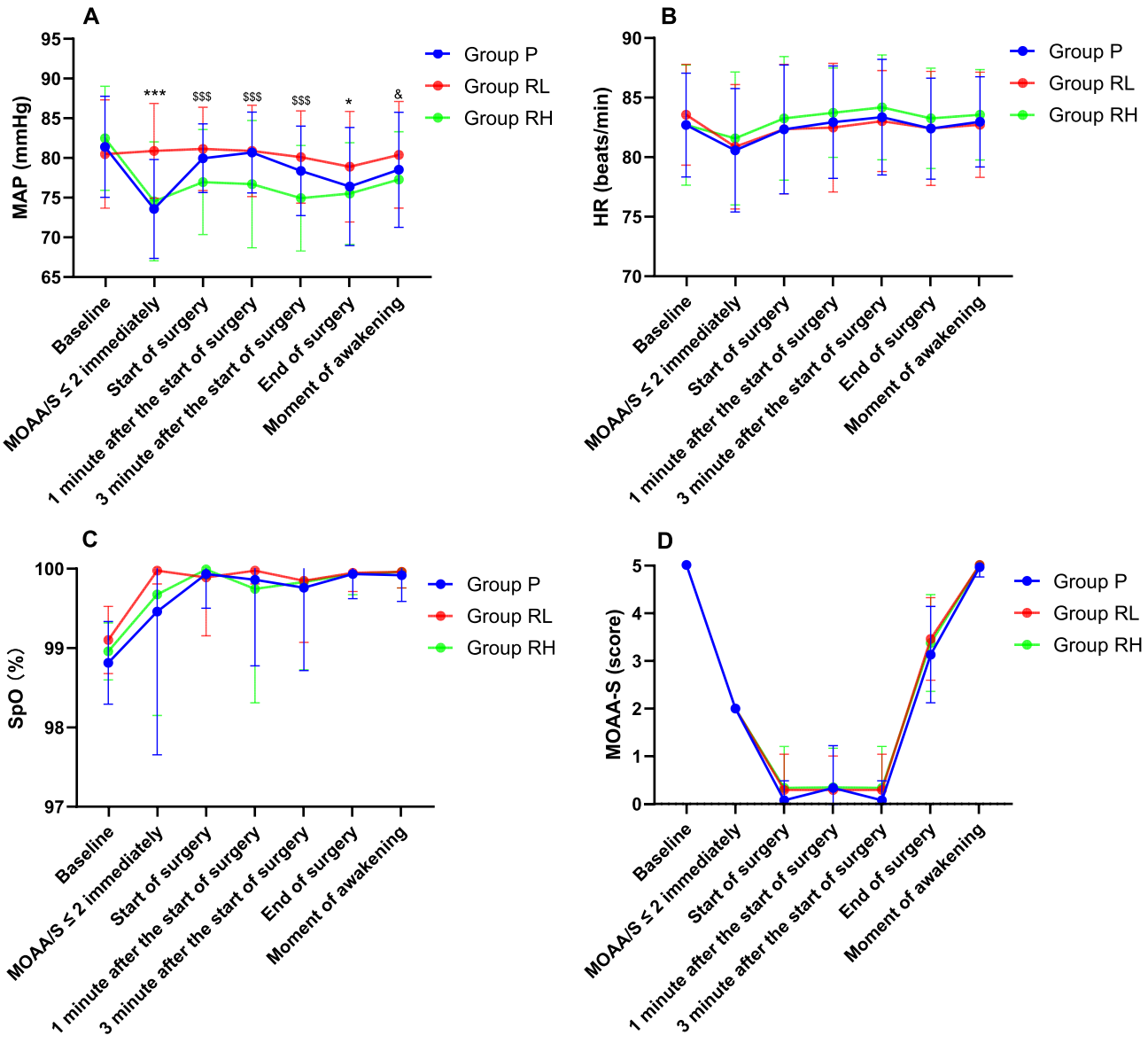

Figure 2 Vital signs at different time points between the three groups. (**A**) MAP at different time points between the three groups; (**B**) HR at different time points between the three groups; (**C**) SpO_2 at different time points between the three groups; (**D**) MOAA-S score at different time points between the three groups.
Notes: ***P < 0.005, *P < 0.05 vs group RL; $^{\$\$\$}$P < 0.005 vs group RH; $^{\&}$P < 0.05 for group RL vs group RH.
Abbreviations: Group P, 2 mg/kg propofol group; Group RL, 0.2 mg/kg remimazolam group; Group RH, 0.3 mg/kg remimazolam group; MAP, mean arterial pressure; HR, heart rate; SpO_2, Oxygen saturation; MOAA-S, Modified Observer's Assessment of Alertness/Sedation Scale.

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The incidence of hypotension was significantly lower in Group P and the RL group compared to the RH group ($P < 0.05$), with no significant difference between Group P and the RL group. The incidences of nausea/vomiting and psychotomimetic symptoms were significantly lower in the RL and RH groups than in the propofol group ($P < 0.05$), with no significant difference between the RL and RH groups. No statistically significant differences were observed among the three groups in the incidences of hypertension, respiratory depression, body movement responses, or injection pain (Table 3).

Recovery time and time to achieve discharge criteria were significantly shorter in the RL Group compared to Group P and the RH Group ($P < 0.05$), with no significant difference between Group P and the RH Group. Group P had significantly more patients requiring propofol supplementation and a higher frequency of additional doses compared to the number of patients and frequency of supplemental doses of RT in the RL and RH Groups ($P < 0.05$). No significant difference in RT supplementation was observed between the RL and RH Groups. Patient satisfaction in Group P was significantly lower than in the RL and RH Groups ($P < 0.05$). No significant differences were found among the three groups regarding anesthesia induction time, operative duration, awakening time, VAS scores at discharge, surgeon satisfaction, or anesthesiologist satisfaction (Table 4).

Table 3 Adverse Events Observed During the Procedure

Variable	Group P (n=70)	Group RL (n=70)	Group RH (n=70)	χ^2	*P*-value
Hypotension, n (%)	1 (1.4)	0 (0)	5 (7.1)	7.206	0.027$^{\$}$
Hypertension, n (%)	2 (2.9)	0 (0)	1 (1.4)	2.029	0.363
Hypoxia, n (%)	5 (7.1)	1 (1.4)	2 (2.9)	3.379	0.185
Somatic motor reactions, n (%)	19 (27.1)	13 (18.6)	11 (15.7)	3.041	0.219
Nausea and Vomiting, n (%)	9 (12.9)	2 (2.9)	3 (4.3)	6.582	0.037$^{\#}$
Potential psychiatric symptoms, n (%)	8 (11.4)	1 (1.4)	1 (1.4)	10.290	0.006$^{\#}$
Injection pain, n (%)	2 (2.9)	1 (1.4)	1 (1.4)	2.029	0.363

Notes: Variables presented as n (%). $^{\#}P < 0.05$ vs Group P, $^{\$}P < 0.05$ vs Group RH, Chi-square test and Fisher' s exact test were used for data analysis.
Abbreviations: Group P, 2 mg/kg propofol group; Group RL, 0.2 mg/kg remimazolam group; Group RH, 0.3 mg/kg remimazolam group.

Table 4 Surgery Time, Anesthesia Time, Recovery Time, Time to Meet Discharge Criteria, Frequency of Additional Propofol or Remimazolam Dose, VAS Pain Score Upon Awakening, VAS Pain Score at Discharge, Patient Satisfaction, Surgeon Satisfaction and Anesthesiologist Satisfaction in the Study

Variable	Group P (n=70)	Group RL (n=70)	Group RH (n=70)	F/χ^2	*P*-value
Anesthesia induction time(min)	1.53 ± 1.11	1.55 ± 0.15	1.54 ± 0.11	0.441	0.644
Surgery time (min)	10.86 ± 3.04	10.51 ± 2.84	10.54 ± 3.19	0.277	0.759
Recovery time (min)	10.19 ± 3.30	8.99 ± 3.60	10.44 ± 3.81	3.282	0.040*
Time to meet discharge criteria (min)	12.57 ± 2.55	11.33 ± 1.32	12.80 ± 2.11	10.374	<0.001*
Frequency of additional propofol, n (%)	23 (32.9%)	15 (21.5%)	11 (15.7%)	9.757	0.045$^{\#}$
1	17 (24.3%)	13 (18.6%)	11 (15.7%)		
2	6 (8.6%)	2 (2.9%)	0 (0%)		
VAS pain score upon awakening (score)	2.01 ± 0.83	2.33 ± 0.68	2.17 ± 0.82	2.877	0.059
VAS pain score at discharge (score)	1.44 ± 0.79	1.31 ± 0.47	1.37 ± 0.54	0.764	0.467
Patient satisfaction, n (%)	57 (81.4%)	67 (95.7%)	66 (94.3%)	10.058	0.007$^{\#}$
Surgeon satisfaction, n (%)	54 (77.1%)	63 (90.0%)	61 (87.1%)	4.940	0.085
Anesthesiologist satisfaction, n (%)	49 (70.0%)	59 (84.3%)	54 (77.1%)	4.051	0.132

Notes: Variables presented as mean ± SD and n (%). *P < 0.05 vs Group RL, $^{\#}$P < 0.05 vs Group P, F-test, Chi-square test and Fisher' s exact test were used for data analysis. P-value is the Bonferroni correction value.
Abbreviations: Group P, 2 mg/kg propofol group; Group RL, 0.2 mg/kg remimazolam group; Group RH, 0.3 mg/kg remimazolam group; VAS, Visual Analogue Scale.

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Discussion

This study conducted a prospective, randomized, double-blind, controlled trial assigning patients to propofol, low-dose remimazolam (RT), and high-dose RT groups. It represents the first systematic evaluation of the efficacy and safety of RT combined with esketamine in painless abortion procedures while exploring the optimal RT dose. The findings demonstrated that low-dose RT (0.2 mg/kg) combined with esketamine offered significant advantages over both the propofol and high-dose RT (0.3 mg/kg) groups in hemodynamic stability, postoperative recovery time, and adverse event control, providing critical evidence-based insights for optimizing ambulatory surgery anesthesia protocols.

The ΔMAP in the low-dose RT group (RL) was significantly lower than that in the propofol (*P*) and high-dose RT (RH) groups, indicating superior intraoperative hemodynamic stability. This outcome is closely related to RT's pharmacological profile. As a novel benzodiazepine, RT induces sedation by selectively enhancing $GABA_A$ receptor-mediated inhibitory neurotransmission, with minimal impact on vascular smooth muscle, thereby reducing blood pressure fluctuations.[14,18] Additionally, esketamine's potent analgesic effect complements RT's sedative properties, collectively mitigating surgical stress responses.[16,19] Notably, the high-dose RT group showed a significantly higher incidence of hypotension than the other groups, suggesting that excessive dosing may diminish RT's hemodynamic benefits and highlighting the critical importance of precise dose titration.[20]

Regarding postoperative recovery, the RL group had significantly shorter recovery times and time to achieve discharge criteria compared to both the propofol and RH groups. This benefit arises from RT's ultra-short-acting pharmacokinetics, including a short half-life and metabolism independent of hepatic and renal function,[21,22] and esketamine's mild impact on respiratory depression.[23,24] In contrast, propofol's high lipophilicity predisposes it to adipose tissue accumulation, potentially delaying recovery.[25] Moreover, the RL and RH groups exhibited significantly lower incidences of nausea, vomiting, psychotomimetic neuropsychiatric symptoms, and hypoxemia than the propofol group, further validating the safety advantages of RT-based regimens. While esketamine can induce psychotomimetic symptoms,[11] the results suggest that RT may counteract these adverse effects.

These findings align with prior research on remimazolam's use in short procedures like gastrointestinal endoscopy, confirming that its combination with esketamine improves hemodynamic stability and shortens recovery.[17,19] However, unlike previous fixed-dose studies (typically using 0.3 mg/kg RT), this trial establishes 0.2 mg/kg as the first evidence-based optimal RT dose for painless abortion - a critical advancement given this procedure's particular susceptibility to hemodynamic fluctuations. This addresses a significant research gap in RT dose-response relationships for gynecological procedures. The significantly lower patient satisfaction in the propofol group, consistent with known issues of propofol-induced injection pain and postoperative discomfort.[26,27] This further supports RT as a clinically superior option for ambulatory abortion care.

Despite rigorous design, this study has limitations. The population was limited to ASA class I–II patients with BMI 18–28 kg/m^2, restricting generalizability to patients with severe comorbidities or obesity. Additionally, as a single-center trial, potential selection bias cannot be excluded; however, potential bias from rotating surgical teams was addressed by standardized operating protocols across all teams. Future multicenter studies are warranted to validate these findings, explore RT combined with other analgesics to optimize anesthesia, and employ pharmacokinetic-pharmacodynamic (PK-PD) modeling to precisely quantify RT's dose-response relationship across different surgical contexts.

Conclusion

This study demonstrates that low-dose remimazolam (0.2 mg/kg) combined with esketamine significantly improves hemodynamic stability, shortens postoperative recovery time, and reduces perioperative adverse reactions during painless abortion. Compared to propofol-based regimens, this combination provides enhanced safety profiles and superior patient comfort, establishing it as a preferred anesthesia strategy for ambulatory abortion procedures. While these findings support immediate clinical adoption, extended follow-up studies are required to validate long-term safety outcomes and potential rare adverse effects. Future research should focus on multi-center validation across diverse populations, investigation of extended applications in other short gynecological procedures, and development of personalized dosing protocols to optimize risk-benefit ratios in comorbid patients.

Abbreviations

RT, Remimazolam tosilate; MAP, mean arterial pressure; HR, heart rate; VAS, visual analogue scale; NMDA, N-methyl-D-aspartate; $GABA_A$, γ-aminobutyric acid subtype A; ASA, American Society of Anesthesiologists; BMI, body mass index; ECG, electrocardiogram; NIBP, noninvasive blood pressure; SpO_2, peripheral oxygen saturation; MOAA/S, Modified Observer's Assessment of Alertness/Sedation.

Data Sharing Statement

The datasets generated during and/or analyzed during the current study are not publicly available due to privacy policies protecting human subjects but are available from Jiejuan Chen (2274860532@qq.com), upon reasonable request.

Ethical Approval and Consent to Participate in the Study

This study was conducted in accordance with the principles of the Declaration of Helsinki and Good Clinical Practice guidelines. The study protocol was approved by the Ethics Committee of Guizhou Medical University (Ref: 2021163). The study was registered on chiCTR.org website (ChiCTR2100047190). Written informed consent was acquired from all patients.

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Author Contributions

Jiejuan Chen and Jingchao Zhang contributed equally to this work and share first authorship. All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors declare no conflicts of interest in this work.

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