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CLINICAL TRIAL REPORT

Comparison of Remimazolam-Flumazenil and Propofol on Psychomotor Function and Emergence Following General Anesthesia in Surgical Abortion: A Randomized Controlled Trial

Jinye Gu[1,*], Yang Liu[1,*], Xiaoyan Lin[1], Lei Fu[1], Jianbo Liu[1], Bona Sun[2], Xiaoyu Li[3], Bo Lu[3]

[1]Department of Anesthesiology, Zhenhai Hospital of Traditional Chinese Medicine, Ningbo, 315200, People's Republic of China; [2]Department of Gynaecology, Zhenhai Hospital of Traditional Chinese Medicine, Ningbo, 315200, People's Republic of China; [3]Department of Anesthesiology, Ningbo No. 2 hospital, Ningbo, 315010, People's Republic of China

*These authors contributed equally to this work

Correspondence: Bo Lu, Department of Anesthesiology, Ningbo No. 2, Hospital, No. 41, Northwest Street, Ningbo, Zhejiang Province, 315010, People's Republic of China, Tel/Fax +86 574 83870920, Email nblbmz@hotmail.com

Objective: This study aims to compare the recovery profiles of remimazolam combined with flumazenil against those of propofol in patients undergoing painless surgical abortion, focusing on psychomotor function and emergence. Rapid recovery and restoration of psychomotor function are critical for enhancing patient safety and satisfaction in outpatient procedures like surgical abortion.

Methods: A total of 110 patients scheduled for surgical abortion were randomly assigned to either the remimazolam group (Group R) or the propofol group (Group P) in a 1:1 ratio. Both groups received intravenous sufentanil for induction, followed by either remimazolam or propofol. Psychomotor function was assessed using the Digit Symbol Substitution Test (DSST) and Trieger Dot Test (TDT) at 30, 60, and 90 minutes post-anesthesia. Emergence parameters, including time to first eye opening and first verbal response, were recorded. Adverse events and hemodynamic parameters were also monitored.

Results: The DSST scores at 30, 60, and 90 minutes post-anesthesia were similar between the Remimazolam group and the Propofol group (F=50.61, P>0.05, η^2=0.0051). The TDT results were also comparable between the groups at all time points (F=0.12, 0.11 and 0.30, all P>0.05, η^2=0.0002, 0.0003 and 0.0008). At 30 or 60 minutes post-anesthesia, DSST scores or TDT performance were significantly worse compared to preoperative baseline in both groups, indicating reduced psychomotor function (P<0.05). The Remimazolam group showed significantly shorter times to first eye opening (54.48±3.45 s vs 99.22±11.78 s, P=0.0014, *Cohen's d*=5.15) and to obey verbal commands (61.85±3.78 s vs 131.1±12.79 s, P<0.0001, *Cohen's d*=7.34) compared to the Propofol group.The incidence of injection pain and respiratory depression was significantly lower in the remimazolam group (P<0.05), while hiccups were more common. Hemodynamic stability was maintained in both groups, with no significant differences in blood pressure or oxygen saturation (P>0.05).

Conclusion: Remimazolam combined with flumazenil provides faster emergence and comparable psychomotor function to propofol in patients undergoing painless surgical abortion. This combination offers a promising anesthetic profile for procedures requiring quick recovery and minimal postoperative complications.

Trial Registration: ChiCTR2300075375, date of registration: 03/09/2023.

Keywords: remimazolam, flumazenil, propofol, psychomotor function, emergence, surgical abortion, anesthesia recovery

Introduction

Surgical abortion is a prevalent medical procedure for terminating early pregnancies. Given the inherent pain and emotional stress associated with this procedure, a significant number of patients prefer opting for painless options.[1–5] This has created a high demand for anesthetic agents that ensure rapid onset, adequate sedation, exceptional analgesia, brief recovery time, and minimal side effects. Propofol is currently the most commonly used

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intravenous anesthetic for painless surgical abortion due to its rapid onset and recovery profile. However, its dose-dependent respiratory and circulatory depression, as well as injection site pain, limit its use in certain populations. These limitations necessitate the exploration of alternative anesthetic agents.

Remimazolam, a novel ultra-short-acting benzodiazepine, has shown considerable promise in this regard.[6–8] Recent studies have highlighted its effectiveness and safety for general anesthesia and sedation, with a sedative efficacy comparable to that of propofol.[9,10] Approved for procedural sedation by the China Food and Drug Administration in December 2019,[11–14] remimazolam offers several clinical advantages: it is rapidly hydrolyzed by plasma esterases, has a short half-life of approximately 7.5 minutes, follows first-order elimination kinetics, and its metabolites are pharmacologically inactive.[9,10,15] Additionally, remimazolam provides more stable hemodynamics and does not cause injection site pain, positioning it as a potentially superior alternative to propofol.[16–18]

Patients undergoing surgical abortion are typically young to middle-aged and generally in good health. They often view this procedure as minor and expect a quick and smooth recovery post-anesthesia to resume their daily activities promptly. Hence, the predictability of drug action duration and rapid recovery are crucial for enhancing both patient safety and satisfaction. Combining remimazolam with flumazenil may elevate the standard of "rapid recovery", offering potential advantages in painless surgical abortion procedures and gaining wider acceptance among patients.

Evaluating emergence from anesthesia involves assessing both the speed of awakening and the restoration of psychomotor functions post-awakening. Postoperative readiness for discharge is closely linked to the recovery of psychomotor function following surgery under general anesthesia.[19–25] Psychomotor function is commonly evaluated using various tests, with the Trieger Dot Test (TDT) and the Digit Symbol Substitution Test (DSST) being among the most frequently used. These tests provide a reliable measure of recovery from anesthesia.[25,26] Understanding the timeline for full psychomotor recovery after general anesthesia or sedation is crucial for advising patients on their post-procedure activities and ensuring their overall safety.

Recent studies have shown the efficacy of remimazolam in various surgical settings, but its use in pregnant populations, particularly for surgical abortion, remains underexplored. This study addresses this gap by comparing the psychomotor recovery and emergence profiles of remimazolam combined with flumazenil versus propofol. We hypothesize that remimazolam with flumazenil provides faster psychomotor recovery and emergence.

Methods

Design and Study Subjects

This clinical study was approved by the Ethics Committee of the Zhenhai District Traditional Chinese Medicine Hospital (YJ-NBZH-KYSB-2023-013) and registered in the clinical trial registration centre of China (ChiCTR2300075375). All procedures adhered to the ethical standards of the Institutional and National Research Committee and aligned with the principles of the 2013 Declaration of Helsinki and its amendments or comparable ethical standards. Informed written consent was obtained from all participants before they were enrolled in the study.

Randomization and Blinding

A total of 110 patients scheduled for surgical abortion were randomly assigned by an anesthesiologist (BL), who was not involved in the study, to either the remimazolam group (Group R) or the propofol group (Group P) in a 1:1 ratio. The randomization was performed using computer-generated random numbers, and the allocation sequence was concealed until the time of enrollment to ensure unbiased group assignment. Due to significant differences in the physical characteristics (remimazolam as a powder and propofol as a white emulsion), administration modes, and dosages, only the study subjects, post-anesthesia care unit staff, and evaluators were blinded to the group assignments. The researchers were not blinded.

Inclusion and Exclusion Criteria

Participants were recruited between September 2023 and May 2024 from the Zhenhai District Traditional Chinese Medicine Hospital, all scheduled for surgical abortion. Inclusion criteria required participants to have an American

Society of Anesthesiologists (ASA) status of I or II, be aged between 20 and 40 years, have a body mass index (BMI) of 18–28 kg/m², and be less than 12 weeks pregnant, as confirmed by ultrasound and human chorionic gonadotropin blood tests. Exclusion criteria were: 1) Cardiopulmonary disease, 2) Acute upper respiratory tract infection or recovery period, 3) Liver and kidney dysfunction, 4) Alcohol abuse, 5) Obstructive sleep apnea-hypopnea syndrome (OSAHS), 6) Chronic use of tranquillizers/opioids/antidepressants, 7) Anesthetic drug allergy.

Study Protocol

No premedication was administered to any patients, who fasted from solids for 8 hours, non-clear fluids (eg, milk or beverages containing milk) for 4 hours, clear fluids for 2 hours, and formula milk for 6 hours prior to the operation. Routine monitoring of electrocardiogram (ECG), blood pressure (BP), pulse oxygen saturation (SpO_2), and bispectral index (BIS) was conducted once in the operating room, with oxygen administered at 3 L/min.

For induction, both groups received intravenous sufentanil (Yichang Renfu Pharmaceutical Co., LTD.) at a dose of 0.1 μg/kg. Group R received intravenous remimazolam (Jiangsu Hengrui Pharmaceutical Co., LTD.) at 0.3 mg/kg, while Group P received intravenous propofol (Sichuan Guorui Pharmaceutical Co., LTD.) at 2 mg/kg. Additional doses of remimazolam (0.1 mg/kg) or propofol (1 mg/kg) were administered as needed. Following the initial dose of remimazolam, Group R underwent a 150-second period before assessing the Modified Observer's Assessment of Alertness/Sedation (MOAA/S) score. Both groups proceeded with the placement of the vaginal speculum when the MOAA/S score was <1, marking the start of the surgical procedure. All surgeries were performed by the same surgeon.

For maintenance of anesthesia, Group R received a continuous infusion of remimazolam at 1 mg/kg/h, and Group P received propofol at 4 mg/kg/h, adjusted to maintain BIS values between 40 and 60. Specifically, if patients displayed signs of inadequate anesthesia (eg, movement, sweating, tearing, hypertension, or tachycardia), an additional dose of remimazolam (0.1 mg/kg) or propofol (1 mg/kg) was administered as appropriate for the respective group. In the event that the SpO_2 drops to 92%, the mandible was lifted or an oxygen mask was utilized for supplemental ventilation. If the average arterial pressure (MAP) falls below 50 mmHg, a norepinephrine dose of 8 μg was administered. Throughout the perioperative period, if the HR drops below 50 beats per minute, atropine at a dose of 0.5 mg was administered.

At the end of anesthesia, Group R were promptly administered 0.2 mg of flumazenil (Zhejiang Ottocon Pharmaceutical Group Co., LTD). If the patient did not open their eyes within 7 minutes, an additional 0.2 mg dose was given.[12]

An investigator (JY G), blinded to group assignments, conducted and recorded the entire recovery process to ensure an unbiased assessment. Throughout the recovery period, excessive stimuli, such as head turning, pillow removal, and bodily movements that could induce pain or oropharyngeal irritation, were avoided to minimize confounders affecting recovery time. Verbal commands, including calling the patient's name and directing them to open their eyes, formed the primary means of assessing patient responsiveness. These verbal stimuli were consistently applied and repeated at regular intervals until the patient complied by opening their eyes.

All patients were then transferred to the Post-Anesthesia Care Unit (PACU) for a minimum of 30 minutes of observation. PACU nurse (XY L), who was blinded to patient group assignments, evaluated patients using the Aldrete score every 5 minutes. Patients were discharged to the ward upon achieving an Aldrete score ≥9.

Outcome Measurement

The primary outcome was psychomotor function, assessed using the Digit Symbol Substitution Test (DSST) score 30 minutes post-anesthesia recovery. Secondary outcomes included DSST assessments at 60 and 90 minutes, along with Trieger Dot Test (TDT) at 30, 60 and 90 minutes.

Additional secondary outcomes included anesthesia emergence parameters such as the time to first eye opening, the time to first verbal response, and the modified Aldrete score, which was measured every 5 minutes in the PACU. Adverse events were also documented, including anesthesia-related issues such as injection pain, nausea, intraoperative awareness, vomiting, resedation (defined as a ≥1 point decrease in RASS), and emergence agitation (defined as RASS score ≥3). Respiratory depression was defined as a respiratory rate of fewer than 8 breaths per minute, SpO2 below 90%, or the need for airway support such as jaw thrust or the insertion of an airway adjunct. Pain on injection was assessed using four

options: no pain, verbal report of pain, arm withdrawal, and combined verbal report and arm withdrawal. Patients meeting any of the last three criteria were classified as experiencing injection pain. Hemodynamic parameters were closely monitored at several key time points: T0 (1 minute pre-induction), T1 (1 minute post-induction), T2 (during cervical dilation), T3 (end of surgery), and T4 (15 minutes post-PACU admission).

Psychomotor function was assessed using both the TDT and DSST by a single investigator (YL). The TDT involved connecting 40 dots in 60 seconds, with performance parameters based on the number of dots missed (NDM), maximum distance of missed dots (MDDM), and average distance of missed dots (ADDM).[26] The DSST required matching symbols to numbers according to a coding table within 90 seconds,[25] with higher scores indicating better cognitive function. Baseline psychomotor assessments were conducted on the day before surgery using both tests, administered twice to familiarize participants and establish baseline levels. Postoperative assessments were made at 30, 60, and 90 minutes post-anesthesia recovery.

Statistical Analysis

The primary outcome was psychomotor function, with the DSST score 30 minutes post-anesthesia recovery used for sample size calculation. With α=0.05 (two-sided) and power (1-β) = 0.8, and assuming a 1:1 ratio between experimental and control groups, PASS 15.0 software determined that 42 subjects per group were required to detect a 5-point difference in DSST scores (standard deviation of 8). Allowing for a 20% dropout rate, a minimum of 53 patients per group was required, resulting in a total sample size of 110.

All statistical analyses were performed using Prism 9.5 software (GraphPad Software, San Diego, CA, USA). Continuous variables were described as mean ± standard deviation (SD) for normally distributed data. Normality was assessed using the Shapiro–Wilk test. Independent sample *t*-tests were used for normally distributed continuous variables. Categorical variables were described as frequencies and percentages, with comparisons made using Chi-square tests or Fisher's exact tests. To evaluate the practical significance of the results, effect sizes were calculated as follows: For continuous variables with group comparisons, Cohen's d was calculated to quantify the magnitude of differences; For repeated measures data, η^2 (Eta Squared) was used to assess the proportion of variance explained by group differences.

Psychomotor function was evaluated using repeated measures ANOVA to compare DSST and TDT results at 30, 60, and 90 minutes post-anesthesia. Mauchly's test checked sphericity, and the Greenhouse-Geisser correction was applied if sphericity was violated. Post-hoc tests used Bonferroni correction. Physiological parameters were similarly analyzed using repeated measures ANOVA. Statistical significance was set at $P<0.05$.

Results

Patient Characteristics, Surgery, and Anesthesia

Out of the 133 patients initially assessed for eligibility, 110 patients were ultimately included in the study, with 55 patients in each group (Propofol group and Remimazolam group) (Figure 1). A total of 23 patients were excluded for the following reasons: 11 patients did not meet the inclusion criteria, and 12 patients declined to participate. Demographic and baseline characteristics, including age, height, weight, and BMI, were similar between the groups with no significant differences (Table 1). The duration of surgery was comparable between the groups, while the duration of anesthesia was significantly longer in the Remimazolam group (596.1±37.69 s) compared to the Propofol group (449.8±24.91 s, P=0.0016). This difference is attributed to the protocol in the Remimazolam group, where a 150-second period was required after the initial dose before assessing the MOAA/S score.

Psychomotor Function

The DSST scores at 30 minutes post-anesthesia were similar between the Remimazolam group and the Propofol group. Similarly, DSST scores at 60 and 90 minutes showed no significant differences between the groups (F=50.61, $P>0.05$, η^2=0.0051) (Figure 2D). The TDT results, including the NDM, MDDM, and ADDM, were also comparable between the groups at all time points (30, 60, and 90 minutes post-anesthesia), with no significant differences observed (F=0.12, 0.11 and 0.30, all $P>0.05$, η^2=0.0002, 0.0003 and 0.0008) (Figure 2A–C).

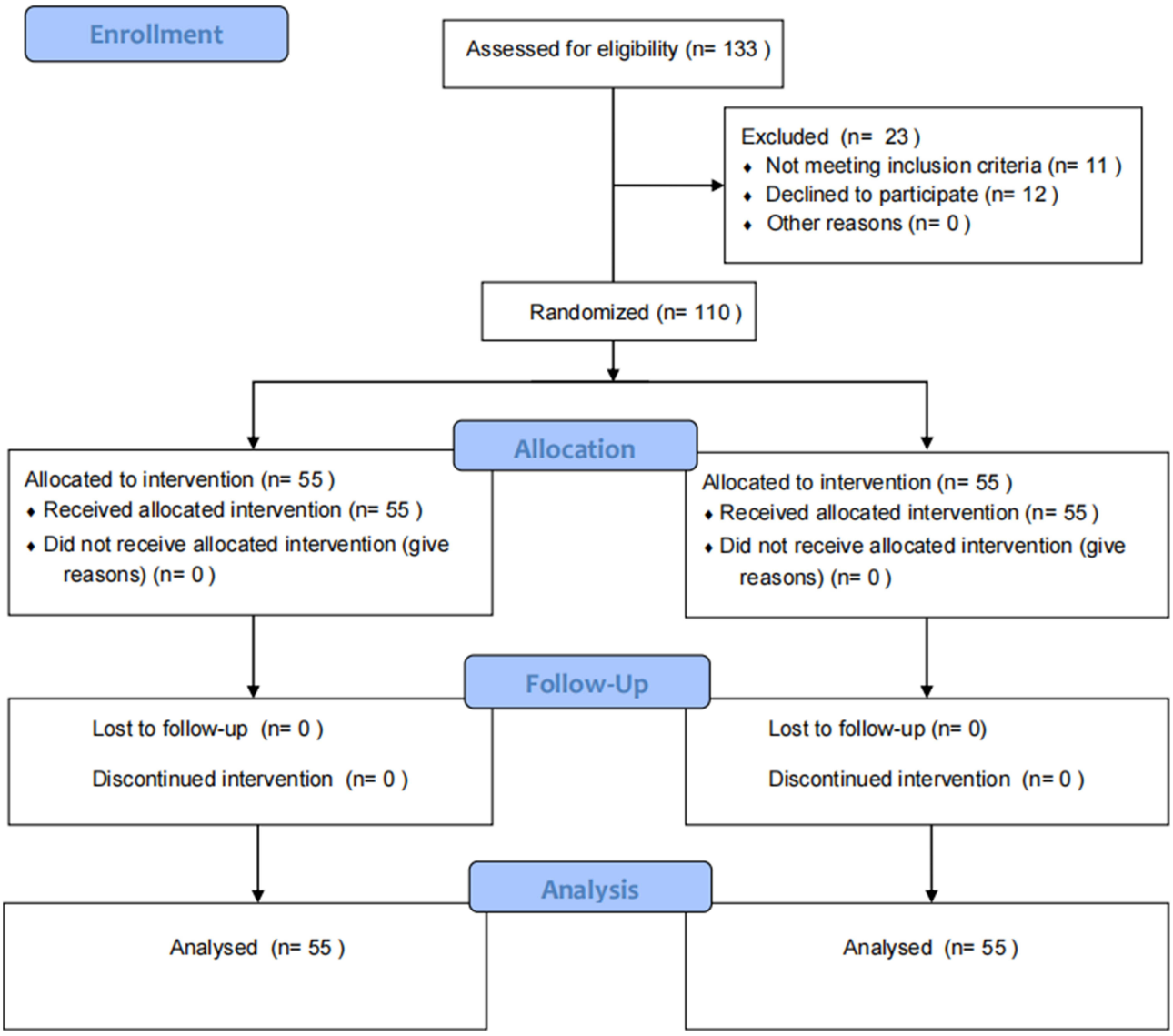

Figure 1 CONSORT diagram.

However, at 30 or 60 minutes post-anesthesia, DSST scores or TDT performance (NDM, MDDM, and ADDM) were significantly worse compared to preoperative baseline in both groups, indicating reduced psychomotor function ($P<0.05$) (Figure 2A–D). This trend was consistent across all measured parameters, suggesting that psychomotor function had not fully recovered to baseline levels at these early postoperative time point.

Emergence Profiles

The emergence profiles showed significant differences between the two groups (Table 2). The time to first eye opening was significantly shorter in the Remimazolam group (54.48±3.45 s) compared to the Propofol group (99.22±11.78 s, $P=0.0014$, Cohen's d=5.1546). Similarly, the time to obey verbal commands was significantly shorter in the Remimazolam group (61.85±3.78 s) compared to the Propofol group (131.1±12.79 s, $P<0.0001$, Cohen's d=7.3431). The effect size, as measured by Cohen's d, indicating an extremely large effect size. This suggests that the difference between the two groups is not only statistically significant but also clinically meaningful, with minimal overlap between the two distributions.

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Table 1 The Characteristic of Patients, Surgery, and Anesthesia

Variable	Propofol (n=55)	Remimazolam (n=55)	P-Value
Age, year	31.95±0.74	31.29±0.69	0.5188
Height, cm	1.589±0.0067	1.589±0.0055	0.9999
Weight, kg	57.46±1.18	56.39±0.94	0.4811
BMI, kg/m^2	22.72±0.41	22.33±0.35	0.4599
ASA PS			
I	46 (83.64%)	43 (78.18%)	0.4667
II	9 (16.36%)	12 (21.82%)	0.4667
Hypertension	3/55 (5.45%)	5/55 (9.09%)	0.7161
Diabetes mellitus	0/55 (2%)	0/55 (0%)	0.9999
Smoking	0/55 (0%)	0/55 (0%)	/
Duration of surgery, s	408.6±23.65	479.4±37.75	0.1152
Duration of anesthesia, s	449.8±24.91	596.1±37.69	0.0016

Notes: Data are expressed as mean±SD, or number (%).
Abbreviations: BMI, body mass index; ASA PS, the American Society of Anesthesiologists physical status.

Upon arrival at the PACU, 83.6% of patients in the Remimazolam group satisfied the discharge criteria compared to 58.2% in the Propofol group (P=0.0059) (Table 2). All patients in both groups met the discharge criteria after 15 and 30 minutes.

No patients in either group experienced re-sedation, emergence agitation, or intraoperative awareness (Table 2). Additionally, no patients in the Remimazolam group required additional flumazenil.

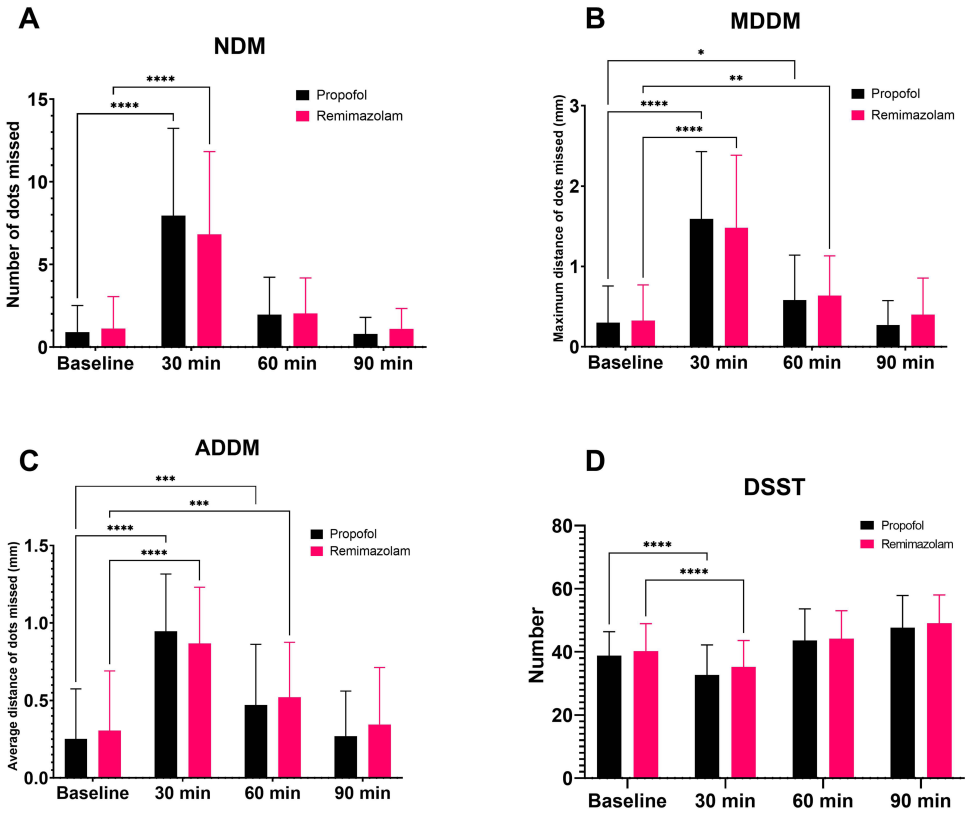

Figure 2 Effects of propofol and remimazolam on Psychomotor function. (**A**) NDM, (**B**) MDDM, (**C**) ADDM, and (**D**) DSST. Measurements were taken at baseline, 30 minutes, 60 minutes, and 90 minutes post-anesthesia. Data are presented as mean ± standard deviation. *P<0.05, **P<0.01, ***P<0.001, and ****P<0.0001.
Abbreviations: NDM, Number of Dots Missed; MDDM, Maximum Distance of Dots Missed; ADDM, Average Distance of Dots Missed; DSST, Digit Symbol Substitution Test.

Table 2 Emergence Profiles

Variable	Propofol (n=55)	Remimazolam (n=55)	P-Value
Time to first eye opening (s)	99.22±11.78	54.48±3.45	0.0014
Time to obey verbal command (s)	131.1±12.79	61.85±3.78	<0.0001
Patients satisfying PACU discharge criteria (Modified Aldrete score ≥ 9)			
Upon arrival(%)	32/55(58.2%)	46/55(83.6%)	0.0059
After 15 min(%)	55/55(100%)	55/55(100%)	/
After 30 min(%)	55 /55(100%)	55/55(100%)	/
Emergence-related side effects			
Re-sedation(%)	0/55 (0%)	0/55 (0%)	/
Emergence agitation(%)	0/55(0%)	0/55 (0%)	/
Patients who experienced intraoperative awareness(%)	0/55 (0%)	0/55 (0%)	/
Additional flumazenil	/	0/55 (0%)	/

Notes: Data are expressed as mean±SD, or number (%).
Abbreviation: PACU, post-anesthesia care unit.

Table 3 Secondary Outcomes

Variable	Propofol (n=55)	Remimazolam (n=55)	P-Value
Injection Pain	12/55 (21.8%)	0/55 (0%)	0.0002
Rescue drug	2/55 (3.64%)	1/55 (1.82%)	0.9999
Hypotensive event	6/55 (10.9%)	2/55 (3.64%)	0.2706
Bradycardia	2/55 (3.64%)	0/55 (0%)	0.4954
Respiratory depression	9/55 (16.4%)	1/55 (1.82%)	0.0162
Hiccup	0/55 (0%)	7/55 (12.7%)	0.0128
Patients who needed vasoactive medication	0/55 (0%)	0/55 (0%)	/
Nausea	5/55 (9.09%)	4/55 (7.28%)	0.9999
Vomiting	2/55 (3.64%)	2/55 (3.64%)	0.9999

Notes: Data are expressed as mean±SD, or number (%).

Secondary Outcomes

The incidence of injection pain was significantly higher in the Propofol group (21.8%) compared to the Remimazolam group (0%, P=0.0002). Respiratory depression was significantly more common in the Propofol group (16.4%) compared to the Remimazolam group (1.82%, P=0.0162). Hiccups were observed in 12.7% of patients in the Remimazolam group, while none were reported in the Propofol group (P=0.0128) (Table 3).

The incidence of hypotensive events, bradycardia, nausea, vomiting, and dizziness showed no significant differences between the groups (Table 3).

Physiological Parameters

Heart rate was significantly higher in the Remimazolam group compared to the Propofol group at T1 (P<0.05), T2 (P<0.01), and T3 (P<0.0001) (Figure 3A). There were no significant differences in SBP, DBP, or SpO_2 between the Remimazolam and Propofol groups at any time point (Figure 3B–D).

Discussion

The primary objective of this study was to compare the recovery profiles of remimazolam combined with flumazenil against those of propofol in patients undergoing painless surgical abortion. Our results indicate that remimazolam, when paired with flumazenil, offers distinct advantages over propofol, particularly in terms of faster recovery of consciousness and reduced adverse effects, without compromising psychomotor recovery.

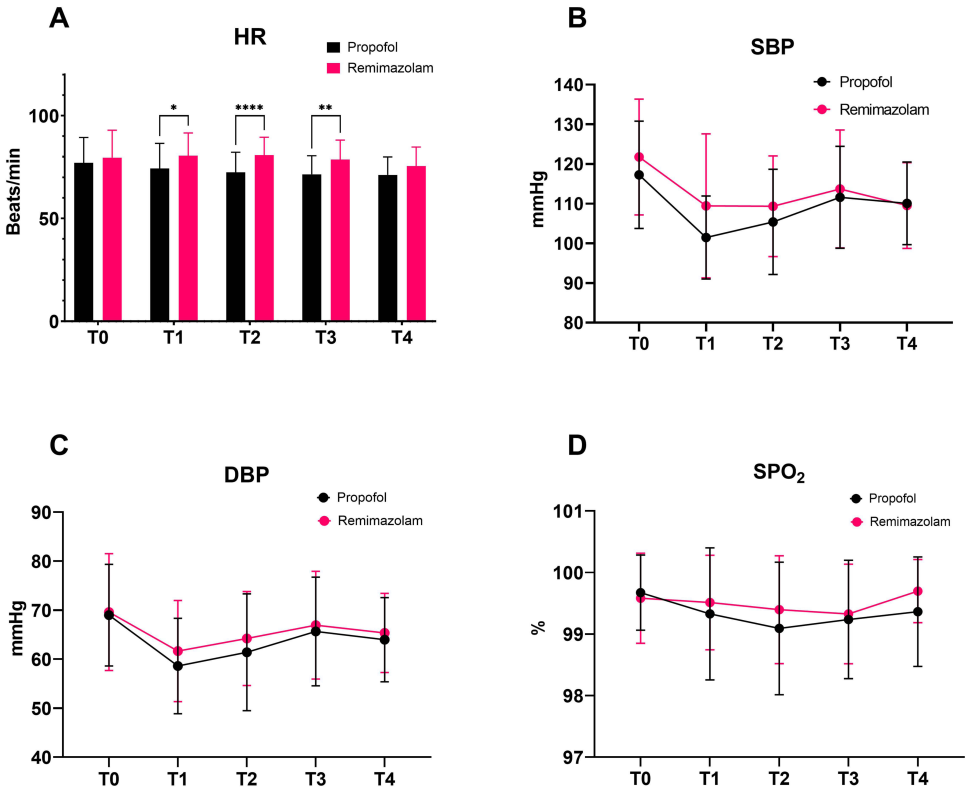

Figure 3 The effects of propofol and remimazolam on various physiological parameters at different time points. (**A**) HR, (**B**) SBP, (**C**) DBP, and (**D**) SpO_2. Data are presented as mean ± standard deviation or median [interquartile range]. * $P<0.05$, ** $P<0.01$, and **** $P<0.0001$.
Abbreviations: HR, Heart Rate; SBP, Systolic Blood Pressure; DBP, Diastolic Blood Pressure; SpO_2, Pulse Oxygen Saturation.

Emergence Profiles

Our study demonstrated significantly shorter times to first eye opening and to obey verbal commands in the Remimazolam group compared to the Propofol group. This rapid recovery of consciousness is crucial for procedures requiring quick patient turnover and minimal postoperative downtime, such as painless abortion. The high percentage of patients in the Remimazolam group meeting discharge criteria upon arrival at the PACU further supports the efficiency of remimazolam in facilitating expedited recovery. These results are consistent with prior studies,[13,27,28] such as those by Lee et al on remimazolam in breast surgery, which also reported faster recoveries.[9] While the differences in time to first eye opening (45 seconds) and time to obey verbal commands (69 seconds) may appear small, they are statistically significant and reflect the unique pharmacokinetic properties of remimazolam. In the context of outpatient procedures like surgical abortion, even minor reductions in recovery time can have practical implications for operating room efficiency, patient turnover, and patient satisfaction. These findings highlight the potential of remimazolam as a viable alternative to propofol, particularly in scenarios where rapid recovery is prioritized.

The ability to reverse remimazolam's effects with flumazenil further enhances its manageability and safety profile, allowing for precise control over sedation levels and faster recovery times. However, re-sedation of remimazolam after flumazenil antagonism has been reported in some cases.[29,30] There is also literature indicating that the use of high doses of flumazenil in the presence of higher doses of remimazolam or in cases of low remimazolam clearance in the body increases the likelihood of re-sedation.[31] Musie's study indicated that a large dose of flumazenil (0.5 mg) is one of the risk factors for re-sedation with remimazolam.[31] It also noted that when the residual concentration of remimazolam is high, the reversal effect of flumazenil may disappear approximately 10 minutes after injection.

In contrast, no re-sedation was observed in our study. All patients recovered successfully after flumazenil antagonism. Several factors may explain this difference. First, the operation times in our study were relatively short, with anesthesia durations averaging only about 10 minutes. Second, our patient population was relatively young, with faster drug metabolism, which likely prevented remimazolam accumulation in the body. Third, we used a lower dose of flumazenil (0.2 mg) for antagonism, which may have reduced the risk of re-sedation.

Psychomotor Function

Psychomotor function was a key focus of this study, assessed using the TDT and the DSST. The TDT test, a widely recognized method for assessing hand-eye coordination post-anesthesia,[23,26,32] is crucial for evaluating fine motor recovery. In the DSST, patients have 90 seconds to match numerical symbols with corresponding legends, testing cognitive and motor functions.[25,33] Our findings indicate that psychomotor function was comparable between the remimazolam and propofol groups at 30, 60, and 90 minutes post-anesthesia. This suggests that both anesthetics allow for a similar rate of recovery in terms of psychomotor function. However, it is important to note that both groups showed significantly reduced psychomotor function compared to preoperative baseline at 30 or 60 minutes post-anesthesia, indicating that full recovery had not been achieved at these early postoperative time points.

Interestingly, despite the rapid emergence profile of remimazolam, the psychomotor function did not show a significant advantage over propofol. This could be attributed to the intrinsic properties of the anesthetics and their effects on the central nervous system. Our results differ significantly from a previously published study by Shimizu et al, which found that psychomotor function (measured by NMD and MDDM scores) was worse in the remimazolam group compared to the propofol group at 30, 60, and 90 minutes post-surgery.[26] However, Shimizu et al's study involved anesthesia durations exceeding 120 minutes. Other studies have cautioned that residual effects of remimazolam can impair psychomotor function up to two hours after administration.[11] In contrast, our study's shorter anesthetic duration (about 10 minutes) might explain the more favorable outcomes for remimazolam seen here.

Hemodynamics and Adverse Events

In the present study, remimazolam was associated with a stable hemodynamic profile, marked by slightly elevated heart rates but no significant differences in blood pressure or oxygen saturation compared to propofol. This stability is a critical factor, as hemodynamic fluctuations can adversely impact patient safety, particularly in outpatient and short-stay procedures.

The significantly lower incidence of respiratory depression and absence of injection pain in the Remimazolam group further highlight its favorable safety profile, making it a potentially preferable choice in settings where these complications can impede patient throughput and comfort. However, the occurrence of hiccups in the Remimazolam group, although minor, represents an adverse event that merits further investigation to elucidate its etiology and clinical significance.[34] Notably, similar hiccup phenomena have been reported with midazolam,[35] suggesting a potential common underlying mechanism that warrants exploration.

Study Limitations

This study has several limitations. First, the study population included only women of reproductive age undergoing surgical abortion, limiting generalizability to other genders, age groups, and procedures. The exclusion of high-risk (ASA III–IV), obese, and elderly patients may also introduce selection bias. Second, the absence of a remimazolam-only group without flumazenil prevents isolating remimazolam's standalone effects on recovery. Third, repeated use of the same DSST test may have introduced a learning effect, potentially improving performance over time. Finally, the 90-minute observation period limits conclusions on longer-term recovery or delayed effects. Future studies with extended follow-up and diverse populations are needed to address these gaps.

Conclusions

In conclusion, our study confirms that remimazolam combined with flumazenil provides faster emergence and comparable psychomotor function to propofol in patients undergoing painless surgical abortion. This combination demonstrates a promising anesthetic profile for procedures requiring quick recovery and minimal postoperative complications, thus serving as a viable alternative to propofol. Future research should focus on broader patient populations, including males and elderly, high-risk groups, and assessing longer-term recovery outcomes to comprehensively validate these findings.

Abbreviations

ASA, American Society of Anesthesiologists; BIS, Bispectral Index; BMI, Body Mass Index; BP, Blood Pressure; DSST, Digit Symbol Substitution Test; ECG, Electrocardiogram; HR, Heart Rate; IQR, Interquartile Range; MAP, Mean

Arterial Pressure; MDDM, Maximum Distance of Dots Missed; MOAA/S, Modified Observer's Assessment of Alertness/Sedation; NDM, Number of Dots Missed; PACU, Post-Anesthesia Care Unit; RASS, Richmond Agitation-Sedation Scale; SBP, Systolic Blood Pressure; SpO_2, Pulse Oxygen Saturation; TDT, Trieger Dot Test.

Data Sharing Statement

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

Ethics Approval and Consent to Participate

This clinical study was approved by the Ethics Committee of the Zhenhai District Traditional Chinese Medicine Hospital (YJ-NBZH-KYSB-2023-013), and it has been registered in the clinical trial registration centre of China (ChiCTR2300075375). All patients were provided with comprehensive information about the study and obtained written informed consent.

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Author Contributions

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 that they have no competing interests.

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