Research Article

Efficacy and Safety of Remimazolam Tosilate Combined with Propofol in Digestive Endoscopy: A Randomised Trial

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Current Knowledge and Objective. Remimazolam tosilate is a novel intravenous sedative of benzodiazepines with no tissue accumulation, which offers a faster onset of action and recovery time than midazolam. The aim of this trial was to compare the efficacy and safety of remimazolam (RM) combined with propofol and traditional propofol in painless digestive endoscopy with painless gastroscopy and colonoscopy.

Methods. Patients were randomised into three groups: RM combined with propofol (RMP group, n = 35), RM (RM group, n = 40), and propofol (P group, n = 38). Each group received 0.1 μg/kg sufentanyl analgesia. An induction dose of 0.1 mg/kg RM and 1 mg/kg propofol was administered to the RMP group, 0.3 mg/kg RM to the RM group, and 2 mg/kg propofol to the P group. Per 5 min, the RMP and RM groups received an additional dose of 0.05 mg/kg RM, while the P group received an extra 0.5 mg/kg propofol. The comparisons involved induction regimen success rate, incidence of hypotension, low pulse rate, injection pain, grade of low oxygen saturation (SpO2), and postoperative adverse reactions.

Results and Discussion. The RMP and P groups’ composition powers were 100%, and the RM group’s composition power was 95% (P = 0.113). The incidence rates of hypotension were 40.0%, 18.4%, and 44.7% in the RMP, RM, and P groups, respectively (P = 0.037). The low pulse incidence rates were 5.7%, 2.6%, and 5.3% in the RMP, RM, and P groups, respectively (P = 0.771). The incidence rates of injection pain were 11.4%, 2.6%, and 26.3% in the RMP, RM, and P groups, respectively (P = 0.007). There was no significant difference in low SpO2 severity scores (P = 0.148). New Findings and Conclusion. Remimazolam tosilate combined with propofol can be used for painless endoscopy, with almost the same safety as propofol. Remimazolam tosilate produces a low incidence of adverse reactions and is a safe anaesthetic option for painless endoscopies.

1. Introduction

Gastrointestinal endoscopic diagnosis and treatment technology have been widely used because of their reliable efficacy; however, they can cause significant discomfort. With the continuous development of medical technology, the demand for patient comfort has gradually increased. Painless gastrointestinal endoscopic diagnosis and treatment and the use of anaesthetic drugs and related technologies, to reduce or avoid possible uncomfortable symptoms in the diagnosis and treatment process, reasonably improve patients’ acceptance, reduce their fear, and create a comfortable medical environment for patients and digestive endoscopists [1].

Propofol is one of the most common drugs for anaesthesia induction and maintenance. Propofol is highly lipophilic, can cross the blood-brain barrier, and is rapidly effective. Its metabolites are excreted by the kidney, are highly controllable, have a short action time, and are fast to awaken and become complete. Its extensive use also involves a high safety profile. However, in high-risk patients, significant cardiovascular inhibition may lead to adverse medical outcomes, and select healthy patients have experienced cardiac arrest when receiving propofol. Propofol
infusion syndrome may also occur when high doses are taken. Lastly, injection pain has become a limitation to the use of propofol.

Remimazolam (CNS7056) is an ultra-short-acting phenyl ester benzodiazepine. It can be rapidly hydrolysed into its inactive carboxylic acid metabolite CNS7054 by liver esterase [2], which allows the early recovery of cognitive function compared to midazolam and provides both predictable and controllable sedative effects [3]. However, it also shows the familiar pharmacological characteristics of classical benzodiazepine drugs and the spectrum of adverse reactions [4, 5].

Many factors, such as age, sex, race, ethnicity, weight, and American Society of Anesthesiologists (ASA) classification of physical status (ASA I: A normal healthy patient; ASA II: A patient with mild systemic disease; ASA III: A patient with severe systemic disease; ASA IV: A patient with severe systemic disease that is a constant threat to life; ASA V: A moribund patient who is not expected to survive without the operation; ASA VI: A declared brain-dead patient whose organs are being removed for donor) and obesity status have relatively small effects on remimazolam. Additionally, this compound presents no damage to hepatocytes in vitro. Compared with propofol, remimazolam causes limited cardiovascular and respiratory depression, less injection pain, and a safe and effective reversal of flumazenil that might alter routine procedural sedation. Remimazolam may also be more beneficial for high-risk patients, although its sedative depth and long-term sedation effects are lower [6–11].

To help determine a better sedation regimen, we compared the efficacy and safety of remimazolam tosilate combined with propofol, remimazolam tosilate, and propofol. The results of exploring whether remimazolam combined with propofol is safer and more effective could provide a single dose reference for future studies.

2. Methods

2.1. Ethics and Registration. This prospective, randomised, single-blind, parallel-controlled study was initiated by the investigator and approved by the Human Research Ethics Committees of the affiliated hospital (2021 YLJSD009). The study protocol was registered in the Chinese Clinical Trials Registry (https://www.chictr.org.cn, ChiCTR2200060510). Written consent was obtained from each participant or their legal representative before enrolment in the study. The investigators conducted the clinical trial at Changzhou Hospital, Jiangsu Province, in accordance with the Declaration of Helsinki (revised in 2013) and the Principles of Good Clinical Practice.

2.2. Study Participants. Patients who participated in the study met the following inclusion criteria: 18–70 years of age; undergoing gastrointestinal endoscopy (gastroscopy and colonoscopy); American Association of Anesthesiologists (ASA) classification grade I or II; body mass index (BMI) of 18–30 kg/m²; and informed consent completion. Patients were not eligible due to any of the following factors: communication disorder; extra drug use outside of the preoperative preparation regimen for a variety of reasons; women during pregnancy or lactation; history of severe motion sickness; severe vertigo and sleep apnoea syndrome; difficult airway; clear refusal to participate; history of drug abuse; alcohol abuse in the previous 2 years; and history of general anaesthesia within 1 month prior to the study or an operation within 1 month was planned. Participants were selected for an anaesthesia appointment for a painless digestive endoscopy and signed an informed consent form. Their personal information was also collected at this time.

2.3. Randomization and Grouping. Investigator PZ generated the random allocation sequence and randomised the patients into three groups: remimazolam combined with propofol (RMP group), remimazolam (RM group), and propofol (P group). Both the patient and endoscopic doctor were unaware of the grouping. In addition, the appearances of remimazolam and propofol were different. Therefore, the drug administration investigator, LC, was aware of the grouping.

2.4. Progression. According to the gastrointestinal endoscopic diagnosis and treatment routine, patients abstained from consuming food and drink before. Open the venous access in the preparation room. In the endoscopy room, the right-hand pulse rate (PR), left upper limb blood pressure (systolic blood pressure (SBP)/diastolic blood pressure (DBP)), and right-hand oxygen saturation (SpO₂) were continuously monitored and recorded. Each patient underwent nasal catheter oxygen inhalation with a controlled oxygen flow of approximately 3–5 L/min [9].

In this study, remimazolam (remimazolam tosilate for injection produced by Jiangsu Hengrui Pharmaceutical Co., Ltd., batch number: 210510AK), a propofol medium, and long-chain fat emulsion injection (Yangtze River Pharmaceutical Group Co., Ltd., Sinopharm H20213012) were used.

All three groups received 0.1 μg/kg sufentanyl analgesia. An induction dose of 0.1 mg/kg remimazolam and 1 mg/kg propofol was administered to the RMP group, 0.3 mg/kg remimazolam to the RM group, and 2 mg/kg propofol to the P group. Patients received an additional dose of 0.05 mg/kg remimazolam in the RMP and RM groups or 0.5 mg/kg propofol in the P group per 5 min [12–15]. The gastroscope operation began when the score for the Modified Observer’s Assessment of Alertness/Sedation (MOAA/S) scale was ≤1 (Supplementary File Table 5). Sedation administration complied with an individualised principle (if the endoscopic standard was met before the intended administered dose was reached, the actual administered dose was recorded, and the examination started; if the total amount of induction is reached but the lens access requirements cannot be met, additional doses should be administered until the depth of sedation is sufficient). If the patient still had physical movement and obvious swallowing movements, the corresponding drug was administered again until sedation was
achieved, and the next administration was postponed for 5 min. If extra doses were given more than five times within 15 min, satisfactory sedation could not be offered, a sedation failure was recorded, and midazolam was used as a sedation remedy.

2.5. Observation Indicators. The primary observational indicator was the success rate of the three induction schemes. Secondary observation indicators included PR, SBP/DBP, and SpO2; adverse events such as low PR, hypotension, and low SpO2 occurring during the process; the dose of atropine and ephedrine used during the study; bucking and body movement scores during examination; onset time; offset time; time to discharge; incidence of injection pain; dizziness severity scores; headache; vomiting; fatigue; abdominal pain; ventosity; active bowel voice; and increased exhaust; and times of advanced doses and time of first defaecation.

2.6. Scoring Criteria. During anaesthesia (from induction until postanaesthesia care unit (PACU) departure), 0.3 mg inatropine was administered when the PR was lower than 55 times/min, signalling low PR. When the mean arterial pressure (MAP) decreased by more than 20% of the baseline value, indicating hypotension, 6 mg ephedrine was administered. If SpO2 ranged from 95–100%, zero points were recorded. When SpO2 fell to 90–95%, 1 point was recorded, and 2 points were given for a drop to 80–90%. In these cases, the patient’s mandibular angle was raised and oxygen flow treatment inhalation was increased or positive pressure was masked to provide oxygen. For an SpO2 below 80%, equating to 3 points, the endoscopic operation was stopped and rescue of respiratory suppression was prepared for. Body movement/bucking Grade: 0, no; 1, slightly movement/mild cough, without affecting the examination, without additional dose; 2, obvious movement/bucking, affecting the examination and required additional doses; 3, failed to cooperate/SpO2 was decreased, suspend examination until enough anesthesia.

Time metrics included onset time (from sedative drug injection to MOAA/S≤ 1), examination time, offset time (from the last dose to patient awakening), and time to discharge (from the last dose to the patient’s Aldrete score of 8 using the Modified Rete Scoring System). The visual analogue scale (VAS) was used to assess patient pain and satisfaction; the WHO Evaluation Criteria for patient nausea and vomiting; Modified European Vertigo Rating Form for dizziness; and the Christensen Postoperative Fatigue Rating Scale for fatigue (Supplementary File). Gastrointestinal discomfort symptoms, such as active bowel sounds and increased exhaustion, were recorded according to Gastrointestinal Symptoms Rating Scales (GSRS). The GSRS contains many symptoms and its corresponding scoring criteria (1 point for normal/no discomfort; 2 points for slightly elevated discomfort that did not affect normal work and life without interventional treatment; 3 points for obvious discomfort, interfering with normal work and life; and 4 points for serious adverse reactions seriously interfering with normal work and life).

2.7. Statistical Analysis. The sample size of this study was calculated based on the incidence of hypotension under propofol anaesthesia [14] using an Online Sample Size Calculator (https://powerandsamplesize.com/Calculators/). The estimated sample size of 35 patients in each group provided a null hypothesis of 90% confidence, with an equal proportion of rejection. Given the 20% shedding rate, a final sample size of at least 133 patients was required; 139 patients were recruited for this study.

3. Results

3.1. Patient Demographics and Baseline Characteristics. Doctor HY enrolled participants and assigned them to the interventions. A total of 139 participants were recruited, and 26 were excluded. Two patients refused to participate, and six did not meet the inclusion criteria (two had low body weight, one was overweight, one was undergoing chemotherapy, one had severe vertigo and sleep apnoea syndrome, and one had a planned gynaecological operation 2 days later). Eighteen patients were lost to follow-up, and 113 were included in the statistical analysis (Figure 1). There was no significant difference in the general data among the three groups (Table 1).

3.2. Primary Outcome. The primary outcome of the study was the success rate within the three groups. There were no remedies in the RMP and P groups; 40 cases were included in the RM group, two of which involved the use of remedial drugs, with a success rate of 95%. There was no significant difference in three-component powers (P = 0.113).

3.3. Secondary Outcomes. The incidences of adverse cardiovascular events included hypotension, low PR, and low SpO2 (SpO2 < 95%). The incidence of hypotension was 40.0% in the RMP group, 18.4% in the RM group, and 44.7% in the P group (P = 0.037; RM vs. P, P = 0.048). The incidence of low PR was 5.7% in the RMP group, 2.6% in the RM group, and 5.3% in the P group (P = 0.771). Low oxygen saturation severity scores were assessed in this study, with no significant difference among the three groups (P = 0.148). The incidence of injection pain was much lower in the RM group than that in the RMP and P groups (RM, 2.6%; RMP, 11.4%; P, 26.3%; P = 0.007; RM vs. P, P = 0.008) (Table 2).
The incidences of hypotension and respiratory depression in the PACU showed no clinically significant differences between the groups \((P > 0.05)\).

There were significant differences in SBP and DBP among the groups \((\text{SBP}; P = 0.002; \text{DBP}; P = 0.004)\). In addition, the RM group was more hemodynamically stable than the other groups \((\text{SBP after induction: RMP}, 113.09 \pm 13.30 \text{mmHg}; \text{RM}, 120.37 \pm 15.73 \text{mmHg}; \text{P}, 108.74 \pm 12.93 \text{mmHg}; \text{DBP after induction: RMP}, 72.63 \pm 10 \text{mmHg}; \text{RM}, 78.34 \pm 9.83 \text{mmHg}; \text{P}, 70.76 \pm 10.37 \text{mmHg}; \text{SBP vs. RMP}, P = 0.08; \text{RM vs. P}, P = 0.001; \text{DBP: RM vs. RMP}, P = 0.051; \text{RM vs. P}, P = 0.004)\) (Table 3). Remimazolam reduced the use of vasoactive drugs \((P = 0.014)\). The mean \(\pm\) SD dose of ephedrine \((\text{RMP}, 4.11 \pm 5.2 \text{mg}; \text{RM}, 1.42 \pm 3.5 \text{mg}; \text{P}, 4.42 \pm 5.9 \text{mg}) \text{RM vs. RMP}, P = 0.038; \text{RM vs. P}, P = 0.031)\) differed significantly among the groups. The scores for dizziness, abdominal pain, and abdominal distension were similar between each group (Table 4).
Continuously measured vital signs, MAPs, and PRs were also analysed. There were no statistically significant differences in any of the vital signs among the three groups ($P > 0.05$). Furthermore, no clinically significant differences were found with regard to onset time ($P = 0.153$) or offset time ($P = 0.296$), and there were no statistically significant differences among the groups in terms of time to discharge ($P = 0.05$). The durations of the gastrointestinal endoscopic examinations were almost the same between all three groups ($P > 0.05$) (Table 4).

The body movement scores, bucking degree scores, and times of advance administration were significantly different among the three groups (body movement score: $P = 0.0322$; RM vs. P, $P = 0.0401$). Bucking degree score: $P = 0.0007$; RMP vs. RM, $P = 0.0025$; RM vs. P, $P = 0.0044$. Advanced administration: $P = 0.0110$; RM vs. P, $P = 0.0099$ (Figure 2). Analysis showed no clinically meaningful differences in the endoscopic satisfaction score ($P = 0.052$), patient satisfaction score ($P = 0.428$), or administered investigator satisfaction score ($P = 0.833$).

Patients had almost the same sleep quality before the examination and on the first, third, and seventh days after the examination ($P > 0.05$). After anaesthesia, adverse reactions, such as fatigue, dizziness, headache, nausea, and vomiting, were not significantly different among the three groups ($P > 0.05$). Gastroscope-related discomfort symptoms, such as abdominal pain, abdominal distension, active bowel sounds, and increased exhaust, were comparable among the groups ($P > 0.05$).
4. The group of propofol (P)
3. The group of remimazolam (RM)
2. The group of remimazolam combined with propofol (RMP)

The group of propofol tosilate combined with propofol (RMP)
The group of remimazolam tosilate (RM)
The group of propofol (P)

Figure 2: Comparison of body movement and bucking degree and times of advance administration (comparison among groups). Each point represents one patient receiving the corresponding score or advance times. Points with different shapes represent different groupings. Body movement/bucking grade: 0, no; 1, slightly movement/mild cough, without affecting the examination, without additional dose; 2, obvious movement/bucking, affecting the examination and required additional doses; 3, failed to cooperate/SpO₂ was decreased, suspend examination until enough anesthesia.

* P < 0.05; ** P < 0.01; *** P < 0.001; **** P < 0.0001.

Compared to the preoperative conditions (baselines), the patients’ degree of fatigue was significantly higher postexamination on the same day (P < 0.0001) and was slightly better on the first day after examination (P = 0.0338); it was similar to baseline values on the third and seventh days after examination (Figure 3(a)). The bowel voice was active, exhaustion was increased post-examination on the same day (P < 0.0001), and symptoms disappeared after the first day (Figures 3(b) and 3(e)). One patient was significantly dizzier than at baseline at the end of the examination (P = 0.0017), and their return visits did not significantly differ on the first, third, and seventh days (P > 0.05) (Figure 3(c)). Postoperative nausea and vomiting (PONV) increased postexamination on the same day (P = 0.0002) (Figure 3(d)). At the same time, ventosity and exhaust scores also increased postexamination on the same day, returned to baseline levels on the first day, and symptoms disappeared on the third and seventh days after examination (Figure 3(f)).

Abdominal pain scores increased postexamination on the same day compared to preoperative baseline values. The scores decreased on the third and seventh days after examination, compared to preoperative baseline values (baseline values: 0.53 ± 1.29 vs. postexamination on the same day: 1.07 ± 1.59, P = 0.004; vs. the first day: 0.48 ± 1.05, P = 0.624; vs. the third day: 0.17 ± 0.66, P = 0.001; and vs. the seventh day: 0.15 ± 0.678, P = 0.001). There was no significant difference in time of first defaecation between the three groups (P = 0.089); the mean for the RMP group is 2.55 ± 0.88 days after examination, and those for the RM and P groups are 2.16 ± 1.4 days and 2.68 ± 1.23 days, respectively (Figure 4).

4. Discussion

Previous studies have shown that the sedation success rates of 0.10, 0.15, and 0.20 mg/kg induction doses of remimazolam were 32%, 56%, and 64%, respectively, and increased with the opioid analgesic fentanyl (92% in the remimazolam group and 75% in the midazolam group) [16]. Remimazolam had synergistic effects with opioid analgesics [17], along with the same result as the current study in that the RM group’s sedation success rate was 95%. We found that during the combined induction of anaesthesia, an additional intra-operative dose of remimazolam, similar to that in the RM group, could achieve sufficient sedation. Although the induction dose of remimazolam in the RMP group was lower than that in the RM group, remimazolam can provide basic sedation whether used respectively or in combination with propofol.

The adverse reaction profile of remimazolam was largely consistent with the other classic benzodiazepines, including common changes in blood pressure and heart rate, decreased respiratory rate, and vomiting, the incidence of which was comparable to that of midazolam [18, 19]. This study found that the inhibitory effect of remimazolam on the cardiovascular system was lower than that of propofol, but this advantage was obviously weakened when combined with propofol, which may be due to an inappropriate drug-dosage ratio. More studies are needed to explore rational drug-dosage ratios and achieve better dosing regimens. It has been reported that the safety profile of remimazolam in high-risk patients (ASA III, IV) is similar to that in low-risk patients; thus, selecting remimazolam rather than propofol for induction is preferred [9, 11].

When gastroenteroscopy was induced by remimazolam anaesthesia, the incidence of bucking was higher than that in the other two groups (RM, 31.6% > P, 7.9% > RMP, 5.7%), and additional medication was needed. Low SpO₂ adverse events in the RM group were mostly associated with patient bucking, which was different from the respiratory depression associated with propofol. This may be because the remimazolam induction dose of 0.3 mg/kg was improper for all patients or because the sedation with remimazolam was not as deep as that with propofol. Drug administration researchers have found that some elderly patients were able to undergo sufficient sedation with a remimazolam dose of 0.2 mg/kg, while younger patients (especially women) experienced obvious agitation and coughing when gastroscopy was introduced at a remimazolam dose of 0.3 mg/kg. Even when additional doses were added, a few patients (two young women) could not complete the diagnosis and treatment operation and received remedial midazolam. However, none of the patients were recalled after surgery at the 7-day visit. Previous studies have shown that the sensitivity of elderly patients to sedation with benzodiazepines has increased [20]. Young women require higher doses of medication, possibly due to oestrogen affecting the GABA receptor in the
hippocampus and in other regions of the limbic system [21]. For midazolam, the plasma clearance is 11% higher in women than in men [17].

Onset times of the three groups were similar, indicating a remimazolam effect as rapid as propofol’s in clinical anaesthesia. The node of the investigator’s recording time was a patient score of MOAA/S \( \leq 1 \), and even if patients in the RM group reached the sedation standard, some patients still coughed during engagement with the microscope, and additional doses were needed to meet the operational requirements. Furthermore, this study revealed that there was no significant difference in the offset time of anaesthesia between the three groups. The time to discharge is ordered as follows: RM > RMP > P, and the difference among the groups was not significant \( (P = 0.05) \). Thus, expanding the experimental sample size may yield positive results. These findings may also stem from painless endoscopy being a shorter procedure, which might not be enough to produce significant differential results; if remimazolam was applied to the induction and maintenance of general anaesthesia, it might lead to delayed awakening compared to propofol [22, 23]. Most previous studies have included gastroscopy or colonoscopy alone, while the participants included in the current study underwent both gastroscopy and colonoscopy at the same time, and the operation and turnover times were longer. Based on the results of this study, we concluded that the application of remimazolam in shorter surgeries does not affect the awakening and recovery of patients and has no adverse effect on PACU turnover.

It has been reported that propofol might be slightly better for PONV than remimazolam [6, 24]. In this study, the incidence of PONV in the RM group (7.9%) was slightly higher than that in the RMP and P groups (5.9% and 2.6%, respectively). One patient who received remimazolam had severe PONV, left the PACU after half an hour, and later developed nausea and vomiting symptoms, dizziness, and headaches, accompanied by sweating. However, the patient did not return to the hospital for medical treatment. Return visits revealed that patients felt dizzy and had a headache on the first day. Symptoms significantly improved on the third day, but slight discomfort was still experienced after a month. As the final statistics did not differ among the three groups, this might be due to the small sample size of this study. Additionally, some reports have suggested that remimazolam causes a slightly higher incidence and severity of nausea and vomiting than propofol. Further studies are needed to evaluate the incidence of PONV after remimazolam treatment [25]. One patient who received...
remimazolam reported increased fatigue compared to propofol for gastroenteroscopy in the last year, despite not being aware of the use of remimazolam. Recently, it was shown that remimazolam can prevent emergent delirium in children following tonsillectomy and adenoidectomy under sevofurane anaesthesia [26]. In the current study, patients still had hypotension after entering the PACU; however, there was no significant difference in the incidence among the three groups. Oxygen saturation was maintained at >94% under oxygen absorption.

The first defaecation of patients in the RM group occurred slightly earlier than that in the other two groups. In this study, it was found that the times of the first normal defaecation in the RM group (a small amount of defaecation) were not noted on the day of diagnosis and treatment. It was also slightly earlier than that in the RMP and P groups. Even if the gap was not statistically significant, did remimazolam promote intestinal peristalsis? Is it more suitable for general surgeries? Few relevant studies on the prevention of postoperative gastric paralysis and intestinal paralysis have been conducted to date.

Patients’ uncomfortable symptoms, such as abdominal distension, increased exhaustion, and active bowel sounds, mostly disappeared on the second or third day, and the original discomforting symptoms returned to pre-examination conditions on the third day. Sleep status after the examination was basically the same in all three groups. Sleep duration increased significantly on the day of treatment, which was consistent with patient fatigue.

Symptoms such as dizziness, headache, nausea, vomiting, and fatigue did not differ among the three groups. Gastrointestinal symptoms such as abdominal pain, abdominal distension, active bowel sounds, and increased exhaustion occurred similarly among the groups, indicating that the potential promoting effect of remimazolam on the digestive tract was mild and did not cause excessive discomfort in patients.

After their examination, patients experienced obvious abdominal pain on the same day. At the return visit by telephone on the next day, abdominal pain was significantly improved. On the third and seventh days, abdominal pain was improved compared to the preoperative basic condition. The improvement might have been caused by most patients who had preoperative abdominal pain taking the relevant drugs for treatment on the third day after examination. However, it is also possible that anaesthetic drugs or gastrointestinal endoscopy can improve abdominal pain, but no relevant study has investigated long-term abdominal pain before and after gastroscopy and colonoscopy.

It is currently believed that tolerance and dependence occur with classical benzodiazepines at prolonged high doses, and none of the participants showed rapid tolerance in this study [27]. The oral bioavailability of remimazolam is extremely low (1.1–2.2%), and it has a bitter taste. The intranasal pathway’s bioavailability of the powder preparation was increased (almost by 50%), but it can cause significant discomfort and pain; thus, the possibility of harm was set to be extremely low [28, 29]. Additionally, none of the weekly
postoperative visits indicated dependence. Flavonoids, fatty acids, and alcohol can inhibit the major metabolic enzymes of remimazolam recombining human carboxylestase1 [30], thereby increasing exposure to remimazolam [29, 31]. Patients with preoperative alcohol or related drug consumption were excluded from this study.

Limitations of this study included its single-centre nature, the small experimental sample size, and the lack of universality that might influence the experiment findings. There was also only one dose ratio between remimazolam and propofol, and no further exploration. Moreover, in the combination regimen, the various adverse effects were not significantly different from those of propofol. However, this study proved that remimazolam combined with propofol is feasible for anaesthesia induction, and perhaps a more appropriate dosage ratio could be advantageous. Lastly, some of the selected patients were examined in the morning and others in the afternoon, and differences in the durations of fasting might have affected their blood pressures.

5. Conclusions

Remimazolam tosylate combined with propofol can be used for gastrointestinal endoscopic diagnosis and treatment, with almost the same safety as propofol. Remimazolam tosylate contributes to a low incidence of adverse reactions and is a safe anaesthetic option for painless endoscopies.

Abbreviations

RM: Remimazolam
CNS7056: Carboxylic acid metabolite of remimazolam
CNS7054: Remimazolam
ASA: American Society of Anesthesiologists (ASA)
BMI: Body mass index
SBP: Systolic blood pressure
DBP: Diastolic blood pressure
MAP: Mean arterial pressure
SpO₂: Oxygen saturation
PACU: Postanaesthesia care unit
PR: Pulse rate
MOAA/S: Modified observer’s assessment of alert
VAS: Visual analogue scale
WHO: World Health Organization
GABA: Gamma-aminobutyric acid receptor
PONV: Postoperative nausea and vomiting
CES1: Recombinant human carboxylesterase 1.

Data Availability

The data used to support the findings of this study are available from the author upon reasonable request.

Ethical Approval

The study was approved by the Human Research Ethics Committees of The Affiliated Changzhou No. 2. People’s Hospital of Nanjing Medical University, Changzhou, China.

Consent

All authors agreed to publish this study.

Conflicts of Interest

The authors declare that they have no conflicts of interest.

Authors’ Contributions

LC and QC conceptualized the study. LC and PZ curated the data. Formal analysis was performed by LC. HY and LC performed the investigation. HY performed the project administration. KS was responsible for software. HY was responsible for supervision. LC was responsible for writing of the original draft, reviewing, and editing. All authors read and approved the final manuscript.

Supplementary Materials

Table s1: The MOAA/S score System; Table s2: Modified Aldrete Scoring System; Table s3: Visual Analogue Scale (VAS); Table s4: WHO Nausea and Vomiting Evaluation Criteria; Table s5: Modified European Vertigo Rating Form; Table s6: Christensen Postoperative Fatigue Rating Scale. (Supplementary Materials)

References
