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REVIEW

Research Progress on the Clinical Application of Remimazolam Outside the Operating Room: A Review of Pharmacological Characteristics, Clinical Effects, and Safety

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Abstract: Remimazolam is a novel ultra-short-acting benzodiazepine sedative, which has shown great promise in clinical scenarios such as outpatient surgeries, endoscopic examinations, intensive care units, and emergency departments due to its rapid onset, adjustable sedation level, and fast metabolic clearance. Currently, there is no consensus on the clinical application of remimazolam in non-operating room anesthesia. This article provides a comprehensive overview of its pharmacological properties and metabolic characteristics, with a particular focus on its application in special populations such as the elderly, patients with high cardiovascular risk, and children. The main purpose is to evaluate its safety and sedative effect in non-operating room settings by comparing it with traditional sedatives, and to provide insights for future research directions, thereby offering theoretical basis and practical guidance for the rational clinical application of this drug outside the operating room.

Keywords: remimazolam, outside the operating room, clinical application, sedation, pharmacological characteristics, special populations

Introduction

In recent years, the landscape of anesthesia practice has witnessed a significant expansion in the utilization of non-operating room anesthesia (NORA), reflecting the growing complexity and diversity of cases managed outside traditional operating rooms. However, the NORA patient population often includes individuals with complex comorbidities and varying degrees of physiological vulnerability, which pose unique challenges in sedation and anesthesia management. The heterogeneity of procedures and patient factors necessitates tailored anesthetic approaches that ensure efficacy, safety, and rapid recovery while minimizing adverse events.[1] Within this evolving clinical context, remimazolam has demonstrated significant potential as an effective agent in the fields of anesthesia and sedation. Unlike traditional sedative drugs, remimazolam has unique pharmacokinetic properties, allowing for rapid titration and predictable sedation depth, and reversible with flumazenil, thereby shortening the postoperative recovery time.[2] This pharmacological advantage makes remimazolam a promising candidate for a variety of clinical applications, including surgical sedation and general anesthesia, where rapid patient recovery is required.[3,4]

This review introduces the pharmacological characteristics of remimazolam and the progress of its clinical research in NORA in recent years, covering potential advantages such as efficacy, hemodynamics, respiratory events, and the recovery process. Additionally, by inferring from intraoperative anesthesia cases in special populations, it clarifies the current status and limitations of the clinical application of remimazolam in NORA practice as well as its future development prospects.

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Pharmacokinetics and Pharmacodynamic Characteristics of Remimazolam

Remimazolam acts on gamma-aminobutyric acid (GABA) receptors, specifically $GABA_A$ receptors. Remimazolam enhances chloride influx through positive allosteric modulation of $GABA_A$ recepter-chloride channel complexes, leading to hyperpolarization of the neuron, resulting in sedation, anticonvulsant activity, and induction of anterograde amnesia.[5] Remimazolam is rapidly metabolized by tissue esterases, allowing a rapid and predictable return to baseline levels of sedation. In addition, remimazolam has a short elimination half-life and a very low risk of drug accumulation which reduces the likelihood of prolonged sedation and its associated complications.[6,7]

Remimazolam is predominantly metabolized by Carboxylesterase 1 (CES1) in the liver, resulting in rapid hydrolysis into its inactive metabolite, CNS7054.[8] This process results in a notably short half-life, usually between 5 to 10 minutes, which facilitates quick recovery from sedation and reduces the likelihood of prolonged effects.[4,9] After hydrolysis, the resulting metabolites can undergo conjugation reactions with endogenous compounds. This promotes the excretion of metabolites through the kidney, which further contributes to the elimination of drugs. The non-organ-dependent metabolism of remimazolam is particularly advantageous. It reduces the risk of drug accumulation in patients with hepatic or renal impairment and makes it a safer option for a broader range of patients, including those with compromised organ function.[10]

Another feature of remimazolam is its rapid onset of action. After intravenous administration, peak plasma concentrations were reached within minutes. Studies have shown that the clearance rate of remimazolam in healthy adults is about 23.0 L/h, and its volume of distribution at steady state (VSS) is 34.8 L, while that of midazolam is 81.8 L.[7,11] This facilitates rapid clearance from the body. The absence of active metabolites ensures that the risks associated with drug accumulation are substantially reduced, thereby improving patient safety during procedures that require sedation.

The context-sensitive half-life (CSHT) of remimazolam, defined as the time required for the plasma concentration of the drug to decrease by 50% after each infusion cessation. At a constant rate infusion of 3h, CSHT of remimazolam was faster than midazolam (7.5 min vs 40 min) but similar to propofol (7.5 min vs 7.5 min).[7] Unlike midazolam, whose CSHT increased with the duration of infusion, remimazolam reached its maximum value after 2 h of constant infusion.

Studies indicate that in pediatric populations aged 2 to 6 years, the pharmacokinetic characteristics of remimazolam, after body size adjustment, are comparable to those in adults. However, differences may exist between children over 6 years of age and adults.[9]

Genetic Polymorphisms and Drug Interactions

The metabolism of remimazolam is notably influenced by genetic polymorphisms, especially those related to the CES1. Studies have shown that genetic variation in CES1 can affect the enzyme activity, thereby affecting the rate of remimazolam metabolism. For instance, the CES1, G143E polymorphism has been shown to impair the metabolic deactivation of remimazolam, resulting in prolonged sedation and variability in drug response among individuals. The identification of these genetic polymorphisms not only aids in understanding interindividual variability in drug metabolism but also highlights the importance of personalized medicine approaches in optimizing remimazolam therapy for different patient populations.[10]

Moreover, drug-drug interactions (DDIs) also play a crucial role in the metabolism of remimazolam. Combination administration of drugs that inhibit CES1 can significantly reduce the metabolic clearance of remimazolam, thereby increasing its plasma concentration and the risk of adverse effects. Clopidogrel may increase plasma concentrations of remimazolam when administered concurrently, potentially enhancing its sedative effects and elevating the risk of respiratory depression or prolonged sedation. Therefore, in surgical and procedural settings requiring sedation, further research is necessary to elucidate the pharmacokinetic profile of remimazolam when administered in combination with other medications. Additionally, standardized management guidelines should be established for patients undergoing multiple therapeutic interventions.[12]

The Application of Remimazolam in Common Diagnosis and Treatment Outside the Operating Room

Endoscopic Examination

The efficacy of remimazolam in painless endoscopy and endoscopic retrograde cholangiopancreatography (ERCP) is supported by multiple studies demonstrating its ability to provide effective sedation while ensuring patient safety. In a study of patients with cirrhosis undergoing endoscopic screening, the median effective dose (ED50) and 95% effective dose (ED95) of remimazolam were 0.097 mg/kg and 0.107 mg/kg, respectively, when combined with sufentanil, underscoring its potency and effectiveness in achieving sedation without significant adverse events.[13] Furthermore, a multicenter randomized controlled trial comparing remimazolam with placebo for upper gastrointestinal endoscopy reported a 91.9% successful sedation rate in the remimazolam group, significantly higher than the 9.1% in the placebo group, underscoring its effectiveness in facilitating endoscopic procedures.[14]

Compared with propofol, remimazolam as an alternative anesthetic agent showed no statistically significant difference in the time to loss of consciousness and recovery time ($P > 0.05$). However, at 5 and 30 minutes after awakening, the Ramsay sedation score of remimazolam was significantly better than that of propofol ($P < 0.05$), indicating improved recovery quality.[15] A Phase III study of the safety and efficacy of remimazolam in colonoscopy showed that patients who received remimazolam required less fentanyl and had better postoperative recovery than those who received placebo or midazolam.[16] Safety profiles also favor remimazolam, as it is associated with a lower incidence of respiratory depression and hypotension compared to propofol, making it a safer option for patients with comorbidities.[17]

Outpatient Surgery

Outpatient surgery aims at patient convenience, quick recovery, and reduced infection and respiratory complications. This imposes higher requirements on the selection of anesthetic drugs. In a randomized clinical trial, 168 patients undergoing outpatient gynecological surgery were included and randomly assigned to the remimazolam group (N=84) or the propofol group (N=84). The results showed that the average Iowa Satisfaction with Anesthesia Scale (ISAS) score in the remimazolam group was 1.7, while that in the propofol group was 2.0 (difference, –0.2; 97.5% confidence interval [CI]: –0.5 to –0.0; $p = 0.02$), indicating non-inferiority.[18]

Moreover, the controllability of sedation depth with remimazolam is a significant advantage. The sedation level can be easily adjusted based on the patient's response, allowing for personalized sedation management during procedures. In studies assessing patient comfort, remimazolam has been associated with high satisfaction scores, indicating that patients often experience less discomfort and anxiety compared to those sedated with other agents.[19] Studies have shown that remimazolam allows for a more tailored approach to sedation, enabling clinicians to achieve the desired level of sedation while minimizing adverse effects. Furthermore, the incidence of postoperative nausea and vomiting following remimazolam administration is lower, which facilitates faster patient recovery.[20]

Bronchoscopy

Bronchospasm is prone to occur during fiberoptic bronchoscopy due to airway hyperresponsiveness. Therefore, while ensuring adequate sedation, it is essential to prevent respiratory depression and maintain hemodynamic stability throughout the procedure.[8] Compared to midazolam, remimazolam has a shorter elimination half-life and is associated with a faster recovery time. A study evaluating the safety and efficacy of remimazolam versus midazolam during bronchoscopy demonstrated that the median time to reach peak sedation (2 min [1–4] vs 3 min [2–5], $p = 0.006$) and the median time from procedure completion to full awakening with remimazolam than midazolam (2 min [1–5] vs 5 min [1–12], $p = 0.035$) were marginally shorter. Moreover, the patient satisfaction in the remimazolam group was significantly higher than that in the midazolam group (median rated scale, 10 vs 7, $p = 0.042$).[21] In a prospective, randomized, double-blind, parallel trial, patients were randomly assigned to receive 0.2 mg/kg of remimazolam and 2 μg/kg of fentanyl citrate, or 2 mg/kg of propofol and 2 μg/kg of fentanyl citrate. The sedation success rate was 99.4% in both groups, demonstrating that the sedative effect of remimazolam was not inferior to that of propofol. Compared with propofol, the median time to loss of consciousness (61 s vs 48 s, $p < 0.001$) and the median time from the end of

bronchoscopy to full awakening (11 min vs 7 min, $p < 0.001$) were slightly longer in the remimazolam group. There was no significant difference in the incidence of adverse events between the remimazolam group and the propofol group (74.8% vs 77.4%, $p = 0.59$). Additionally, the remimazolam group exhibited significantly lower rates of hypotension (13.5% vs 29.7%, $p < 0.001$), hypotension requiring treatment (1.9% vs 7.7%, $p = 0.017$), and injection pain (0.6% vs 16.8%, $p < 0.001$) compared to the propofol group.[22] Compared with dexmedetomidine, remimazolam had a lower rate of procedure interruption (8.2% vs 39.2%, $p < 0.05$) and a lower incidence of oxygen desaturation (14.3% vs 44.2%, $p < 0.05$) in flexible fiberoptic bronchoscopy.[23] Therefore, this makes remimazolam potentially a new alternative for bronchoscopy.

ICU Sedation

The pharmacokinetic profile of remimazolam is also particularly advantageous in the intensive care unit (ICU). Studies have demonstrated that remimazolam can achieve the desired sedation depth significantly faster than midazolam, with mean times to reach target sedation scores being markedly reduced. One study reported a mean time to achieve a Ramsay Sedation Scale score of 3–4 of just 12.6 minutes with remimazolam, compared to 18.4 minutes for midazolam.[24] The ability to quickly adjust sedation levels not only enhances patient comfort but also minimizes the risk of prolonged sedation, which can lead to complications such as delirium and extended ICU stays. This characteristic facilitates swift recovery from sedation when needed, which is particularly important in dynamic ICU settings where prompt patient evaluation.[25] In addition, remimazolam has the favorable characteristics of organ-independent metabolism and minimal accumulation, which makes it particularly suitable for ICU patients with liver or kidney failure.[7]

Research indicates that for critically ill patients requiring prolonged sedation, remimazolam does not increase ICU mortality or the incidence of adverse events when compared to propofol or midazolam.[25,26] Furthermore, remimazolam has a minimal effect on hemodynamic stability and is not associated with propofol-related infusion syndrome. In addition, it allows for a quicker recovery following discontinuation of the infusion compared to midazolam. These findings suggest that remimazolam is both effective and safe for use in long-term sedation of mechanically ventilated patients.[27]

In Emergency Department Procedural Sedation

Recent prospective studies have demonstrated the good safety of remimazolam in procedural sedation in the emergency department (ED). A pivotal prospective study conducted at Aalborg University Hospital compared remimazolam administration by emergency medicine physicians without anesthesiology specialization to that by registered nurse anesthetists experienced with the drug. The study enrolled 103 patients undergoing procedural sedation, with 53 sedated by emergency physicians and 50 by nurse anesthetists. Remarkably, no or only mild respiratory adverse effects were observed in 97% of patients in the emergency physician group and 100% in the nurse anesthetist group, with severe respiratory depression being exceptionally rare. Procedural amnesia rates were similarly high (93% vs 90%), and median time to safe unsupervised discharge was 15 minutes in both groups. These findings affirm that remimazolam can be safely and effectively administered by non-anesthesiology-trained physicians under appropriate training and supervision, expanding its utility in the ED setting.[28]

In a study evaluating remimazolam dosing in the emergency department, researchers administered an initial 7.5 mg dose for sedation, or 5 mg for specific patient groups (eg, age >65 years, American Society of Anesthesiologists (ASA) physical status >3, and body weight <50 kg), and an additional 2.5 mg dose could be administered after 2 minutes. The sedation success rate was as high as 80%, without the need for a second drug, and no serious adverse events were reported. In addition, in the ED, remimazolam is not only suitable for procedural sedation in surgeries such as joint reduction and cardiac cardioversion, but can also be used as an induction drug for tracheal intubation and as a sedative after intubation.[29]

Clinical Application Progress in Special Populations

Elderly Patients

As individuals age, physiological changes such as decreased hepatic and renal function can alter drug metabolism and clearance, thereby increasing the risk of adverse effects from standard sedatives like propofol. Studies have shown that remimazolam demonstrates a more favorable safety profile in this patient population, as it is associated with lower incidences of hypotension and bradycardia compared to propofol. This characteristic is particularly beneficial given that elderly patients are often more susceptible to hemodynamic fluctuations during sedation.[30,31] A study investigated the effects of remimazolam and propofol on elderly patients undergoing hip replacement surgery. The results demonstrated that plasma levels of epinephrine, norepinephrine, and cortisol at 24 and 72 h post-operation, as well as the incidence of adverse reactions, were significantly lower in the remimazolam group compared to the propofol group. Furthermore, Visual Analogue Scale (VAS) scores at all post-operative time points were significantly reduced compared to pre-operative levels in both groups; however, no statistically significant difference was observed between the two groups.[32] A meta-analysis comparing remimazolam and propofol in painless gastroscopy and colonoscopy for elderly outpatients selected 7 RCTs, involving 1499 patients, among whom 764 patients were assigned to receive remimazolam sedation. The results showed that the incidence of adverse reactions was significantly lower in the remimazolam group compared with the propofol group, including hypoxemia, respiratory depression, hypotension, bradycardia and injection pain. There were no significant differences in the incidence of postoperative nausea and vomiting (PONV), headache and dizziness between the two groups.[33]

Research indicates that remimazolam may reduce the incidence of postoperative delirium compared to propofol, which is vital given that delirium can lead to long-term cognitive decline and increased mortality in older adults.[34,35] In a study involving elderly patients undergoing procedures requiring sedation, those treated with remimazolam exhibited stable cognitive function postoperatively, as measured by the Mini-Mental State Examination (MMSE) and Montreal Cognitive Assessment (MoCA) scores, suggesting that remimazolam does not adversely affect cognitive recovery.[36] Moreover, the ability of remimazolam to maintain hemodynamic stability while minimizing cognitive impairment underscores its potential as a preferred sedative for elderly patients undergoing various surgical and procedural interventions. A study exploring the effects of remimazolam on postoperative function, intraoperative hemodynamics and oxygenation in elderly patients undergoing lobectomy showed that on the 7 days after surgery, the Verbal Fluency Test (VFT), Digit Symbol Switching Test (DSST) and Auditory Verbal Learning Test - Huashan (AVLT-H) scores of the remimazolam group were all higher than those of the propofol group. The dose of phenylephrine used intraoperatively in the remimazolam group was significantly lower. Moreover, 60 minutes after one-lung ventilation, the PaO2 and oxygenation index (OI) of the remimazolam group were significantly higher than those of the propofol group, and the intrapulmonary shunt (Qs/Qt) was significantly lower than that of the propofol group.[37] These findings suggest that remimazolam can achieve an anesthetic effect comparable to that of propofol while being safer and significantly improving the recovery quality of elderly outpatients.

High-Risk Cardiovascular Patients

Studies have demonstrated that remimazolam can maintain stable blood pressure and heart rate during anesthesia induction and maintenance, even in patients with severe cardiac conditions, such as those undergoing coronary artery bypass grafting or valve replacement surgery.[38,39] Moreover, a comparative analysis of remimazolam and etomidate in patients undergoing valve replacement surgery showed that remimazolam resulted in significantly lower hemodynamic fluctuations, indicating its superior cardiovascular stability.[40]

In cardiac surgeries, remimazolam has been successfully utilized for sedation in patients with significant cardiovascular comorbidities, demonstrating its capability to provide effective sedation while minimizing hemodynamic disturbances.[41] For instance, a case report highlighted the successful use of remimazolam during a complex cardiac surgery involving cardiopulmonary bypass, where it maintained stable hemodynamics without significant complications.[38] Furthermore, its use in non-cardiac surgeries, such as laparoscopic procedures, has shown similar

benefits, with studies indicating reduced vasopressor requirements and better overall hemodynamic stability compared to traditional agents like sevoflurane.[42] The versatility of remimazolam allows it to be employed in a variety of surgical settings, providing a safe anesthetic option for patients with varying degrees of cardiovascular risk.

Pediatric Patients

Remimazolam has garnered significant attention owing to its distinctive pharmacological characteristics in the context of pediatric sedation. Several studies have demonstrated that remimazolam provides rapid onset of sedation with a favorable safety profile, making it suitable for various pediatric procedures. A randomized clinical trial revealed that remimazolam has a median ED50 of 0.19 mg/kg for loss of consciousness in children, indicating its potency compared to propofol, which had an ED50 of 1.11 mg/kg, making remimazolam approximately 5.8 times more potent.[43] This significantly reduces the anxiety experienced by pediatric patients during endoscopic and imaging examinations conducted outside the operating room, thereby enhancing the accuracy and reliability of these diagnostic procedures.[44] A randomized controlled study investigating the prevention of postoperative delirium in children undergoing tonsillectomy and adenoidectomy under sevoflurane anesthesia found that administration of 0.2 mg/kg remimazolam at the end of surgery significantly reduced the incidence of postoperative delirium compared to 0.9% normal saline. A double-blind randomized controlled trial evaluating the effect of remimazolam on postoperative delirium in children undergoing laparoscopic surgery revealed that both continuous infusion and single bolus administration of remimazolam during the procedure effectively lowered the incidence of postoperative delirium.[43] Furthermore, in pediatric patients undergoing cardiac catheterization, remimazolam was shown to maintain hemodynamic stability while achieving effective sedation without significant adverse events.[45] Notably, remimazolam had no injection pain and greatly improved the comfort of the children. These findings suggest that remimazolam is not only effective but also safe for use in children, with minimal cardiovascular and respiratory depression, which is particularly important in this vulnerable population.

As remimazolam has not yet received approval from the US Food and Drug Administration (FDA) for pediatric use, limited research has been conducted on its application in children. Consequently, its use in this population often occurs off-label. This absence of standardized dosing protocols raises concerns about the potential for variability in individual responses, necessitating careful monitoring and adjustment during administration.[46] Additionally, while remimazolam has been associated with reduced emergence delirium compared to other agents, the evidence remains inconclusive, and further studies are needed to establish its efficacy in this regard across diverse pediatric populations.[47] Moreover, the potential neurotoxic effects of remimazolam, particularly in neonates and young children, warrant further investigation to ensure its long-term safety and impact on neurodevelopment.[48]

Adverse Reactions and Safety

The clinical safety profile of remimazolam has been extensively evaluated across various studies, demonstrating a generally favorable safety profile. Compared to propofol, which are associated with significant cardiovascular and respiratory side effects, remimazolam has shown to be well-tolerated across a diverse patient population, including the elderly and those with comorbidities. Moreover, in studies focusing on procedural sedation, remimazolam exhibited a lower frequency of adverse events, including respiratory depression and hypoxemia, compared to propofol, thereby underscoring its safety advantage in vulnerable populations.[49,50]

In addition, the reversibility of remimazolam is its significant advantage. This is particularly crucial in cases where unexpected complications arise or when patients require immediate recovery from sedation.[51] Therefore, remimazolam holds promise as an alternative to traditional sedatives in various surgical and anesthetic settings.

For adverse effects, most reports were classified as mild to moderate and resolved without intervention. In studies comparing remimazolam to propofol, the incidence of severe adverse events was notably lower in the remimazolam group.[52] The most common adverse events observed include transient hypotension and mild sedation-related symptoms, which were manageable and did not lead to prolonged hospital stays or significant morbidity.[53,54]

Limitations and Future Research Directions

The clinical application of remimazolam, while promising, is constrained by several limitations that warrant careful consideration. One significant challenge is the optimization of dosing and the lack of individualized medication strategies. Furthermore, while remimazolam is known for its rapid onset and short duration of action, its pharmacodynamic properties can vary widely among individuals due to factors such as age, weight, and concurrent medications.

Additionally, the safety data for remimazolam in special populations, particularly children and critically ill patients, remains limited. For instance, although remimazolam has shown efficacy in adult procedural sedation, its use in pediatric anesthesia is still off-label, and there are no established dosing guidelines for this demographic.[43] The lack of robust clinical trials assessing the safety and efficacy of remimazolam in children.

The future of remimazolam research is poised for significant advancements, particularly in the realm of multicenter and large-sample clinical trials. There is a pressing need for robust studies that can provide comprehensive data on the efficacy and safety of remimazolam across diverse patient populations and clinical settings. Large-scale trials are essential to establish standardized dosing regimens, identify potential adverse effects in different demographics, and compare its effectiveness against other anesthetics in varied surgical procedures. Furthermore, multicenter trials can facilitate a more extensive patient recruitment process, ensuring that findings are generalizable and applicable to a broader spectrum of clinical practice.

Exploring new indications for remimazolam and optimizing drug combination regimens also represent promising avenues for future research. While remimazolam has established its role in procedural sedation and general anesthesia, there is potential for its application in other medical contexts. Additionally, research into optimal drug combinations, such as remimazolam with opioids or other sedatives, could enhance sedation quality while mitigating side effects. Understanding the synergistic effects of these combinations will be crucial in developing protocols that maximize patient comfort and safety during procedures. Future studies should aim to assess the pharmacodynamic interactions between remimazolam and other agents, identifying the most effective and safe combinations for various clinical scenarios.

Conclusion

Overall, remimazolam offers rapid onset and predictable recovery, hemodynamic stability, andreversibility with flumazenil, making it a useful option for NORA, particularly for endoscopic and bronchoscopic procedureswhere swift turnover and cardiorespiratory stability are valued. Current evidence suggests comparable efficacy to propofolwith fewer hypotensive and respiratory events in some studies, but data remain limited or mixed in ICU contexts and insufficient in pediatrics and emergency medicine; thus, agent selection should be individualized to patient risk andprocedural needs. Priority research includes larger, multicenter trials by setting and population, with standardized outcomes to clarify where remimazolam confers a consistent advantage.

Disclosure

The authors report no conflicts of interest in this work.

References

1. Finlay JE, Leslie K. Sedation/analgesia techniques for nonoperating room anesthesia: new drugs and devices. *Curr Opin Anaesthesiol*. 2021;34 (6):678–682. doi:10.1097/ACO.0000000000001057
2. Lee A, Shirley M. Remimazolam: a review in procedural sedation. *Drugs*. 2021;81(10):1193–1201. doi:10.1007/s40265-021-01544-8
3. Masui K. Remimazolam: its clinical pharmacology and evolving role in anesthesia and sedation practice. *Curr Opin Anaesthesiol*. 2024;37 (4):344–351. doi:10.1097/ACO.0000000000001384
4. Zhang H, Li H, Zhao S, Bao F. Remimazolam in general anesthesia: a comprehensive review of its applications and clinical efficacy. *Drug Des Devel Ther*. 2024;18:3487–3498. doi:10.2147/DDDT.S474854
5. Kilpatrick GJ. Remimazolam: non-clinical and clinical profile of a new sedative/anesthetic agent. *Front Pharmacol*. 2021;12:690875. doi:10.3389/fphar.2021.690875
6. Wang Z, McCalla Z, Lin L, et al. Impact of genetic polymorphisms and drug-drug interactions mediated by carboxylesterase 1 on remimazolam deactivation. *Drug Metab Dispos*. 2025;53(1):100023. doi:10.1124/dmd.124.001916
7. Kim KM. Remimazolam: pharmacological characteristics and clinical applications in anesthesiology. *Anesth Pain Med*. 2022;17(1):1–11. doi:10.17085/apm.21115

8. Bai C, Xu M, Guo Y, Jin Y, Zhao X. Clinical application and research progress of remimazolam for pediatric patients. *Drug Des Devel Ther*. 2024;18:1221–1229. doi:10.2147/DDDT.S453440
9. Colin PJ, Bichajian LH, Curt VR, et al. Pharmacokinetics and pharmacodynamics of remimazolam for procedural sedation in children and adolescents. *Anesthesiology*. 2025;143(2):368–382. doi:10.1097/ALN.0000000000005560
10. Petersen KU, Schmalix W, Pesic M, Stohr T. Carboxylesterase 1-based drug-drug interaction potential of remimazolam: in-vitro studies and literature review. *Curr Drug Metab*. 2024;25(6):431–445. doi:10.2174/0113892002308233240801104910
11. Schuttler J, Eisenried A, Lerch M, Fechner J, Jeleazcov C, Ihmsen H. Pharmacokinetics and pharmacodynamics of remimazolam (CNS 7056) after continuous infusion in healthy male volunteers: part I. pharmacokinetics and clinical pharmacodynamics. *Anesthesiology*. 2020;132(4):636–651. doi:10.1097/ALN.0000000000003103
12. Petersen KU, Schmalix W, Pesic M, Stohr T. Drug-drug interaction potential of remimazolam: CYP 450, transporters, and protein binding. *Curr Drug Metab*. 2024;25(4):266–275. doi:10.2174/0113892002300657240521094732
13. Cao YH, Chi P, Zhou C, Lv WF, Quan ZF, Xue FS. The 50% and 95% effective doses of remimazolam tosilate with adjuvant sufentanil for sedation in patients with liver cirrhosis undergoing oesophagogastric varices screening endoscopy. *J Clin Pharm Ther*. 2022;47(12):2068–2073. doi:10.1111/jcpt.13751
14. Ichijima R, Ikehara H, Yamaguchi D, et al. Randomized controlled trial of remimazolam compared with placebo in Japanese patients undergoing upper gastrointestinal endoscopy: phase III investigator-initiated clinical trial. *Dig Endosc*. 2024;36(9):995–1002. doi:10.1111/den.14758
15. Yang L, Zhang J, Xiao N, et al. Clinical trial comparing remimazolam with propofol during intravenous anesthesia: a prospective randomised clinical trial. *Comb Chem High Throughput Screen*. 2024;27(10):1544–1550. doi:10.2174/0113862073247219230927050009
16. Rex DK, Bhandari R, Desta T, et al. A phase III study evaluating the efficacy and safety of remimazolam (CNS 7056) compared with placebo and midazolam in patients undergoing colonoscopy. *Gastrointest Endosc*. 2018;88(3):427–437e6. doi:10.1016/j.gie.2018.04.2351
17. Zhang L, Li C, Zhao C, You Y, Xu J. The comparison of remimazolam and midazolam for the sedation of gastrointestinal endoscopy: a meta-analysis of randomized controlled studies. *Afr Health Sci*. 2022;22(2):384–391. doi:10.4314/ahs.v22i2.44
18. Wang XL, Dai LL, Li YN, et al. Comparing remimazolam and propofol for postoperative anesthesia satisfaction in outpatient gynecological surgery: a randomized clinical trial. *Drug Des Devel Ther*. 2024;18:4615–4627. doi:10.2147/DDDT.S483029
19. Zhang L, Wang Z, Liu Y, Zhang X, Wu Y. Comparison of remimazolam tosilate and propofol sedation on the early postoperative quality of recovery in patients undergoing day surgery: a prospective randomized controlled trial. *Drug Des Devel Ther*. 2024;18:1743–1754. doi:10.2147/DDDT.S456675
20. Wei Y, Zhu M, Man Y, et al. Clinical study of flumazenil antagonizing remimazolam on nausea and vomiting after gynecologic day surgery. *Drug Des Devel Ther*. 2024;18:631–638. doi:10.2147/DDDT.S444313
21. Kim SH, Cho JY, Kim M, et al. Safety and efficacy of remimazolam compared with midazolam during bronchoscopy: a single-center, randomized controlled study. *Sci Rep*. 2023;13(1):20498. doi:10.1038/s41598-023-47271-w
22. Zhou YY, Yang ST, Duan KM, et al. Efficacy and safety of remimazolam besylate in bronchoscopy for adults: a multicenter, randomized, double-blind, positive-controlled clinical study. *Front Pharmacol*. 2022;13:1005367. doi:10.3389/fphar.2022.1005367
23. Zhou L, Zou J, Li X, et al. Efficacy and safety of remimazolam versus dexmedetomidine for patients undergoing flexible fiberoptic bronchoscopy: a randomized, clinical trial. *J Clin Anesth*. 2024;99:111677. doi:10.1016/j.jclinane.2024.111677
24. Yang F, Yi S, Xing J, et al. Cost-effectiveness analysis of remimazolam and midazolam in goal-guided sedation in ICU. *Altern Ther Health Med*. 2024:AT10928.
25. Yao Z, Liao Z, Li G, Wang L, Zhan L, Xia W. Remimazolam tosylate's long-term sedative properties in ICU patients on mechanical ventilation: effectiveness and safety. *Eur J Med Res*. 2023;28(1):452. doi:10.1186/s40001-023-01440-9
26. Tang Y, Yang X, Yu Y, et al. Remimazolam besylate versus propofol for long-term sedation during invasive mechanical ventilation: a pilot study. *Crit Care*. 2022;26(1):279. doi:10.1186/s13054-022-04168-w
27. Yang X, Tang Y, Du R, et al. Long-term sedation with remimazolam besylate versus propofol in critically ill patients during invasive mechanical ventilation: a study protocol for a multicenter randomized non-inferior trial. *Front Pharmacol*. 2023;14:1139872. doi:10.3389/fphar.2023.1139872
28. Andreassen S, Nielsen VML, Krarup AL, et al. Remimazolam for procedural sedation in the emergency department: a prospective study of effectiveness and patient satisfaction. *Scand J Trauma Resusc Emerg Med*. 2025;33(1):93. doi:10.1186/s13049-025-01402-6
29. Bradshaw JC, Lester L, Greer MR, Leon DA. Remimazolam: a novel frontier in procedural sedation for emergency medicine. *J Emergency Med*. 2025;79:545–550. doi:10.1016/j.jemermed.2025.09.031
30. Yamaguchi S, Ishida Y, Sasaki T, Higuchi S, Bito K, Oe K. Remimazolam for simultaneous percutaneous mitral valve clip and percutaneous left atrial appendage closure in an elderly patient with impaired cardiac function: a case report. *Clin Case Rep*. 2024;12(7):e9215. doi:10.1002/ccr3.9215
31. Liu X, Zhang L, Zhao L, et al. Comparison of the safety of remimazolam and propofol during general anesthesia in elderly patients: systematic review and meta-analysis. *Front Med*. 2025;12:1409495. doi:10.3389/fmed.2025.1409495
32. Zhang J, Wang X, Zhang Q, Wang Z, Zhu S. Application effects of remimazolam and propofol on elderly patients undergoing Hip replacement. *BMC Anesthesiol*. 2022;22(1):118. doi:10.1186/s12871-022-01641-5
33. Terres MT, Assis ML, Da Silveira CB, Amaral S. Remimazolam versus propofol for endoscopy sedation in elderly patients: a systematic review, meta-analysis and trial sequential analysis. *Minerva Anestesiol*. 2024;90(9):775–784. doi:10.23736/S0375-9393.24.18027-3
34. Fujimoto D, Obata N, Mizobuchi S. Effectiveness of remimazolam in preventing postoperative delirium in elderly patients with proximal femoral fractures. *J Anesth*. 2024;38(4):475–482. doi:10.1007/s00540-024-03339-z
35. Xu Q, Qian J, Zhang SQ, Xia F, Hu HJ, Xiao F. Dose-response study of remimazolam combined with remifentanil for attenuating stress response during laryngeal mask airway insertion in elderly female patients: a prospective double-blinded study. *Drug Des Devel Ther*. 2025;19:1575–1583. doi:10.2147/DDDT.S494426
36. Wang Y, Gou ZH, Wang GM, Ye LH, Chen L, Wang Q. Association of remimazolam with delirium and cognitive function in elderly patients undergoing general anesthesia or procedural sedation: a meta-analysis of randomized controlled trials. *Front Med*. 2025;12:1567794. doi:10.3389/fmed.2025.1567794

37. Kuang Q, Zhong N, Ye C, Zhu X, Wei F. Propofol versus remimazolam on cognitive function, hemodynamics, and oxygenation during one-lung ventilation in older patients undergoing pulmonary lobectomy: a randomized controlled trial. *J Cardiothorac Vasc Anesth*. 2023;37(10):1996–2005. doi:10.1053/j.jvca.2023.06.027
38. Satoh T, Nishihara N, Sawashita Y, Ohno S, Hirata N, Yamakage M. Remimazolam anesthesia for MitraClip implantation in a patient with advanced heart failure. *Case Rep Anesthesiol*. 2021;2021:5536442. doi:10.1155/2021/5536442
39. Sagawa T, Ishida Y, Sasaki T, Hosokawa M, Bito K, Oe K. Anesthesia management using remimazolam for coronary artery bypass grafting and aortic valve replacement in a patient with severe cardiac dysfunction: a case report. *SAGE Open Med Case Rep*. 2024;12:2050313X241310640. doi:10.1177/2050313X241310640
40. Hu B, Zhang M, Wu Z, et al. Comparison of remimazolam tosilate and etomidate on hemodynamics in cardiac surgery: a randomised controlled trial. *Drug Des Devel Ther*. 2023;17:381–388. doi:10.2147/DDDT.S401969
41. Saito K, Ohno S, Maeda M, Hirata N, Yamakage M. Remimazolam anesthesia for cardiac surgery with cardiopulmonary bypass: a case report. *JA Clin Rep*. 2021;7(1):21. doi:10.1186/s40981-021-00424-0
42. Seong H, Cho JE, Yoon SZ, Choi SU. Remimazolam reduces vasopressor use post-induction and during maintenance of general anesthesia in patients undergoing laparoscopic gynecology: a propensity score-matched analysis. *J Clin Med*. 2024;13:21. doi:10.3390/jcm13216407
43. Shen Y, Sun Y, Wang YT, et al. Dose equivalence of remimazolam and propofol for loss of consciousness in pediatric patients: a randomized clinical trial. *Pain Physician*. 2024;27(8):521–528. doi:10.36076/ppj.2024.7.521
44. Yang X, Lin C, Chen S, Huang Y, Cheng Q, Yao Y. Remimazolam for the prevention of emergence delirium in children following tonsillectomy and adenoidectomy under sevoflurane anesthesia: a randomized controlled study. *Drug Des Devel Ther*. 2022;16:3413–3420. doi:10.2147/DDDT.S381611
45. Hosokawa M, Takahashi Y, Ueno T, Oe K, Masui K. Remimazolam anesthesia in pediatric patients undergoing cardiac catheterization for congenital heart disease: a retrospective observational study. *J Anesth*. 2024;38(6):796–805. doi:10.1007/s00540-024-03395-5
46. Ni MJ, Jin YT, Wu QL, et al. Effective dose of intranasal remimazolam for preoperative sedation in preschool children: a dose-finding study using Dixon's up-and-down method. *Front Pharmacol*. 2024;15:1372139. doi:10.3389/fphar.2024.1372139
47. Nitta Y, Kamimura Y, Shiroshita A, Kido K. Concomitant use of intravenous remimazolam with inhalation anesthesia and subsequent emergence delirium in children: a systematic review and meta-analysis. *Cureus*. 2025;17(3):e80044. doi:10.7759/cureus.80044
48. Tang Z, Sun S, Lin Z, et al. Neonatal anesthesia with remimazolam reduces the expression of synaptic proteins and increases depressive behavior in adult mice. *Neurosci Lett*. 2024;842:137971. doi:10.1016/j.neulet.2024.137971
49. Oka S, Satomi H, Sekino R, et al. Sedation outcomes for remimazolam, a new benzodiazepine. *J Oral Sci*. 2021;63(3):209–211. doi:10.2334/josnusd.21-0051
50. Choe JW, Chung MJ, Park SW, et al. Safety and efficacy of remimazolam versus propofol during EUS: a multicenter randomized controlled study. *Gastrointest Endosc*. 2024;100(2):183–191e1. doi:10.1016/j.gie.2024.04.001
51. Wu X, Wang C, Gao H, et al. Comparison of remimazolam and propofol about safety outcome indicators during general anesthesia in surgical patients: a systematic review and meta-analysis. *Minerva Anestesiol*. 2023;89(6):553–564. doi:10.23736/S0375-9393.23.17034-9
52. Swart R, Maes SSA, Cavanaugh D, Mason KP. Remimazolam pilot for office-based dental sedation: adverse events, awareness and outcomes. *J Clin Med*. 2023;12(23):7308. doi:10.3390/jcm12237308
53. Zhang H, Fu M, Yue F, et al. Comparison of the anesthetic effects of remimazolam tosilate and remimazolam besylate in daytime hysteroscopic surgery. *BMC Anesthesiol*. 2024;24(1):382. doi:10.1186/s12871-024-02773-6
54. Chen D, Liao M, Wu XR, Zhao TY, Sun H. Comparison of efficacy and safety of equivalent doses of remimazolam versus propofol for gastroscopy anesthesia in elderly patients. *Sci Rep*. 2024;14(1):7645. doi:10.1038/s41598-024-58294-2