REVIEW ARTICLES

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Remimazolam: a comprehensive review

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Abstract

Remimazolam is a novel, ultra-short-acting benzodiazepine that has emerged as a promising agent in modern anesthetic and intensive care practice. This review presents a detailed analysis of its pharmacokinetic and pharmacodynamic properties, clinical efficacy, and safety profile across various patient populations and procedural contexts. The drug's rapid metabolism by plasma esterases, minimal reliance on hepatic or renal function, and availability of a reversal agent (flumazenil) distinguish it from traditional sedatives such as propofol and midazolam. Clinical data support its utility in procedural sedation, general anesthesia, and ICU sedation, particularly in elderly and hemodynamically unstable patients. Pediatric applications are discussed, highlighting the early evidence and dosing considerations. The review also compares remimazolam with other agents such as propofol and dexmedetomidine, underlining its advantages in cardiovascular stability and recovery profiles. While current results are encouraging, the article emphasizes the need for further research to establish standardized protocols and explore its long-term safety, especially in vulnerable populations.

Key words: pharmacokinetics, elderly patients, procedural sedation, remimazolam, pediatric anesthesia, intravenous anesthesia, ICU sedation.

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Remimazolam is an ultra-short-acting benzodiazepine that has gained increasing popularity in anesthesiology and intensive care in recent years. The growing interest in this drug is partly due to its exceptional controllability – when administered intravenously, it is rapidly metabolized by plasma esterases, resulting in a very short half-life and a predictable therapeutic effect, as its metabolism is independent of renal and hepatic function. Moreover, if necessary, its effects can be reversed with flumazenil, just like any other benzodiazepine. Another key feature that positions remimazolam as a competitor to propofol and dexmedetomidine is its minimal impact on hemodynamic stability in patients receiving the drug. These unique properties make remimazolam a highly attractive alternative for short- and long-term sedation, as well as general anesthesia, compared to currently used intravenous sedatives.

In this article, we summarize the current knowledge regarding the pharmacokinetics and pharmacodynamics of remimazolam, its use in procedural sedation, general anesthesia, and long-term sedation in the intensive care unit (ICU), and we review the literature on its application in pediatric and elderly patient subpopulations.

PHARMACOKINETICS

The development of remimazolam was driven by the idea of creating a sedative agent that combines the properties of two existing drugs: midazolam and remifentanil [1]. Similar to midazolam, remimazolam is a positive allosteric modulator of the GABA-A receptor. By binding to the benzodiazepine site, it enhances the effect of GABA, increasing the frequency of chloride channel opening. The resulting chloride influx hyperpolarizes the neuronal membrane and inhibits central nervous system activity [1–3]. The extraordinary pharmacological properties of remimazolam stem from the incorporation of an ester bond in its structure, similar to remifentanil. Consequently, remimazolam is rapidly hydrolyzed by plasma esterases into an inactive metabolite, producing a fast-acting and short-duration sedative effect with a predictable time course [3].

The pharmacokinetic profile of remimazolam is characterized by a small steady-state volume of distribution, rapid clearance, short context-sensitive half-life, and linear first-order kinetics [4, 5].

Phase I studies compared the pharmacokinetic properties of remimazolam and midazolam. These studies demonstrated that the volume of distribution following intravenous administration of

remimazolam at doses of 0.01–0.30 mg kg^{-1} min^{-1} was approximately 34.8 L, compared to an average distribution volume of 81.8 L for midazolam administered intravenously at 0.075 mg kg^{-1} min^{-1}. Furthermore, the clearance of remimazolam was more than three times higher than that of midazolam (70.3 vs. 20.3 L h^{-1}) and was independent of body mass. The half-life was 0.75 hours for remimazolam and 4.29 hours for midazolam. Similar pharmacokinetic properties were observed with continuous infusion of remimazolam, which was initially administered at a rate of 5 mg min^{-1} for 5 minutes, followed by 3 mg min^{-1} for 15 minutes, and then 1 mg min^{-1} for another 15 minutes [6].

Remimazolam is metabolized by plasma esterases, specifically hepatic carboxylesterase, into an inactive metabolite and excreted in urine [7]. Following intravenous administration, approximately 92% of remimazolam is bound to plasma proteins, mainly albumin [8].

The dose-dependent half-life following a 3-hour infusion of remimazolam was over five times shorter than that of midazolam (approximately 7.5 min vs. 40 min) and comparable to that of propofol (approximately 7.5 min) [9–11].

Pharmacokinetic properties did not significantly differ between younger and elderly individuals (mean age 21.0 years vs. 66.0 years). Similar pharmacokinetic characteristics were observed in patients with normal renal function compared to those with end-stage renal disease (eGFR > 90 vs. < 15) and in patients with normal liver function compared to those with mild to moderate hepatic impairment (Child-Pugh class A and B).

PHARMACODYNAMICS

Remimazolam is a benzodiazepine that binds the benzodiazepine site at the $\alpha+/\gamma-$ interface of the GABA-A receptor and acts as a positive allosteric modulator. In the presence of GABA, it increases the frequency of channel opening and the resulting chloride influx, producing neuronal hyperpolarization and reduced excitability; its activity spans benzodiazepine-sensitive subtypes containing $\alpha1$, $\alpha2$, $\alpha3$, or $\alpha5$, with minimal affinity for α4/α6-containing receptors [8].

Pharmacodynamic analyses of the sedative effects of remimazolam, based on the bispectral index (BIS), electroencephalogram (EEG), Narcotrend index, and Modified Observer's Assessment of Alertness/Sedation (MOAA/S) scale, have demonstrated a rapid onset of short-duration sedation, with depth dependent on dosage. Studies in healthy volunteers showed that a single intravenous dose of 5 mg of remimazolam induced a rapid and short-lasting sedative effect as assessed by the MOAA/S scale [6].

Additionally, intravenous administration of remimazolam at doses of 0.075–0.20 mg kg^{-1} resulted in an earlier onset of sedation, a deeper sedative effect compared to intravenous midazolam at 0.075 mg kg^{-1} (MOAA/S < 2 vs. 3–4), and a shorter average duration of sedation (5–20 min vs. 40 min) [12].

Studies have also revealed that continuous intravenous administration of remimazolam at an induction dose of 0.2 mg kg^{-1} over a 1-minute bolus, followed by an infusion at 1.0 mg kg^{-1} h^{-1} for 2 hours, resulted in deeper sedation and faster recovery compared to continuous midazolam infusion at 0.05 mg kg^{-1} h^{-1} for 2 hours, preceded by an induction bolus of 0.15 mg kg^{-1} over 1 minute [13]. These findings highlight the rapid onset of action, profound sedative effects, and short dose-dependent half-life of remimazolam.

CLINICAL USE: GENERAL ANESTHESIA

Remimazolam has emerged as a potential alternative to propofol in total intravenous anesthesia (TIVA) and as an adjunct to balanced anesthesia. The manufacturer's recommended dosage of remimazolam in general anesthesia is an initial dose of 6–12 mg min^{-1} for induction, followed by 1 mg min^{-1} ("…with a range of 0.1–2.5 mg/min based on clinical judgement…") for maintenance of general anesthesia [14].

To avoid confusion, it should be emphasized that the manufacturer's recommendations are expressed as absolute infusion rates in mg min^{-1}, while clinical trials typically report weight-adjusted regimens in mg kg^{-1} h^{-1}. For clarity, the induction dose of 6–12 mg min^{-1} corresponds to approximately 0.08–0.16 mg kg^{-1} min^{-1} (≈5–10 mg kg^{-1} h^{-1}) in a 70-kg patient, and the maintenance dose of 1 mg min^{-1} corresponds to about 0.014 mg kg^{-1} min^{-1} (≈0.85 mg kg^{-1} h^{-1}). Presenting both formats helps ensure comparability and reduces the risk of misinterpretation in clinical practice.

Available evidence indicates that remimazolam has a longer time to loss of consciousness compared to the most commonly used intravenous anesthetic agent – propofol. A study by Doi *et al*. [15] compared 2 dosing regimens of remimazolam in doses of 6 and 12 mg kg^{-1} h^{-1} with propofol. Regardless of the remimazolam dose, propofol induced a faster loss of consciousness [102.0 s and 88.7 s vs. 78.7 s ($P < 0.0001$ and $P = 0.0149$,)] for the 6 and 12 mg kg^{-1} h^{-1} and propofol groups, respectively. This study also showed a statistically significant increase in time to extubation with remimazolam.

A promising approach to reduce the time to return of consciousness and extubation is to reverse

the effects of remimazolam with flumazenil. A meta-analysis by Wu *et al*. [16] showed an advantage of such a combination over propofol in terms of time to extubation (mean difference = –4.26 min, 95% CI: –6.81 to –1.7, $P = 0.0011$). The meta-analysis also showed fewer episodes of respiratory depression (RR = 0.2, 95% CI: 0.04–0.89, $P = 0.03$). However, when using flumazenil, the possibility of re-sedation should be considered, especially after long infusions of remimazolam. Therefore, patients should be monitored even when the effects of the anesthetic appear to have completely faded. If re-sedation occurs, it is necessary to consider flumazenil re-administration.

The standard approach for monitoring patients undergoing total intravenous anesthesia involves the use of indicators that process EEG recordings, such as the BIS, to assess the depth of anesthesia. However, it is crucial to acknowledge the potential limitations of this method when employing remimazolam, as the databases used to develop the BIS index did not encompass EEG data from patients under remimazolam anesthesia. A study by Zhao *et al*. [17] demonstrated the efficacy of BIS in monitoring the depth of sedation, suggesting its potential for similar applications in the monitoring of general anesthesia. However, further research is necessary to ascertain the validity of this method in this context.

REMIMAZOLAM VS. PROPOFOL

In summary, remimazolam offers recovery advantages primarily when compared with midazolam, while its benefits over propofol are most evident in improved hemodynamic stability and safety outcomes rather than in shorter recovery times.

Importantly, the availability of flumazenil as a reversal agent provides an additional safety net that is not available with propofol [18]. However, when remimazolam is compared directly with propofol in randomized trials and meta-analyses, no statistically significant differences have been observed in recovery-related outcomes such as wake-up time, time to eye opening, or discharge readiness [19–21]. Thus, the advantage of remimazolam over propofol does not lie in faster recovery, but rather in its more favorable safety and tolerability profile.

These features explain why remimazolam provides clearly faster recovery when compared with midazolam and other traditional benzodiazepines.

When comparing remimazolam to conventional anesthetics, such as propofol, several advantages can be identified, including a shorter duration of sedation, reduced cardiovascular depression, and predictable pharmacokinetics. Due to its rapid hydrolysis via ester linkage, remimazolam is metabolized into inactive metabolites without requiring organ-dependent metabolism.

Several meta-analyses have compared these two agents. The conclusions indicate no significant differences in induction time [21] or the depth of sedation achieved with remimazolam [22, 23]. However, studies have reported fewer occurrences of [18–20]: pain during intravenous injection, respiratory depression, post-induction hypotension, and postoperative nausea and vomiting in mixed surgery or endoscopic procedures. No significant differences have been observed between remimazolam and propofol in terms of recovery time, discharge time, or time to eye opening [19–22].

A recent systematic review [24] including 50 randomized controlled trials (RCTs) with 9,193 patients, provides important nuance regarding postoperative nausea and vomiting (PONV). The authors reported no overall difference between remimazolam and other anesthetics for total PONV, but subgroup analyses revealed lower overall PONV compared with volatile anesthetics (RR ≈ 0.50; 95% CI: 0.34–0.73), and higher vomiting rates when compared with propofol (RR ≈ 1.41; 95% CI: 1.05–1.90). These findings highlight that the risk of PONV with remimazolam is strongly dependent on the comparator drug and should not be oversimplified.

A notable finding is a lower incidence of bradycardia with remimazolam compared to propofol in mixed surgical procedures, whereas no significant difference was found in endoscopic procedures. Mao *et al*. [25] reported that patients in the remimazolam group experienced lower physical discomfort and emotional distress on postoperative days one and three compared to those in the propofol group (measured via patient-reported scores for physical comfort, emotional state, physical independence, pain, and psychological support). However, a trial involving elderly patients undergoing orthopedic surgery based on confusion assessment method did not find a significant difference in the incidence of postoperative delirium in the remimazolam group compared to the propofol group [26].

REMIMAZOLAM VS. DEXMEDETOMIDINE

Dexmedetomidine is a unique, selective $\alpha 2$ adrenergic agonist primarily used for sedation and as an adjunct in general anesthesia with co-analgesic properties. To date, only a few studies have compared remimazolam to dexmedetomidine [27–29]. The available evidence suggests that remimazolam leads to a faster onset of sedation in patients undergoing lower extremity surgery under spinal anesthesia.

Studies have reported that remimazolam is associated with a lower incidence of bradycardia and

hypertension, but a higher incidence of respiratory depression compared to dexmedetomidine. Additionally, remimazolam was linked to faster recovery times and higher patient satisfaction scores; however, it also resulted in more episodes of oversedation and prolonged delirium [30].

In a retrospective comparison, Lee *et al*. [29] observed that remimazolam infusion may be associated with a higher risk of postoperative delirium in elderly patients undergoing orthopedic surgery under spinal anesthesia compared with dexmedetomidine.

REMIMAZOLAM IN PROCEDURAL SEDATION

Remimazolam is predominantly used in endoscopic procedures. Its safety profile closely resembles that of midazolam during procedural sedation. However, transitioning from traditional benzodiazepines to remimazolam as the first-choice sedative in clinical practice may take time and require adaptation to modern anesthetic protocols.

A phase III study demonstrated that remimazolam provides effective procedural sedation with a favorable safety profile, characterized by minimal hemodynamic effects, painless intravenous administration, reduced PONV, and rapid neurological recovery [31]. The recovery time was found to be shorter than that of midazolam in sedation for esophageal and gastric endoscopy.

One drawback of remimazolam in procedural sedation is its relatively slow onset of action (1–3 minutes), whereas most diagnostic gastroduodenoscopies last only 2–3 minutes. In one study, approximately 25% of patients were unable to complete a colonoscopy due to inadequate sedation, which was classified as a high failure rate [1].

Children undergoing magnetic resonance imaging (MRI) examinations often suffer from neurological diseases and are treated with various medications. Inhalation sedation with sevoflurane is one of the popular options but is associated with potential contamination of the suite and possible delirium during emergence. Available studies indicate that effective intravenous sedation during the MRI examination is possible [32]. Some authors have suggested that remimazolam may be a suitable sedative for interventional radiology procedures and during MRI [33].

Several trials have compared remimazolam with propofol during procedural sedation. The findings generally favor remimazolam, indicating a better safety profile and sedative efficacy [34–36], with fewer adverse effects such as hypoxia, pain following injection, respiratory depression, and elevated bilirubin levels [37]. However, both remimazolam and propofol showed similar success rates for sedation in colonoscopy patients [34].

A randomized trial confirmed that remimazolam is safe for ASA III and ASA IV patients [38]. Additionally, a scientific report from South Korea concluded that remimazolam is a safe and effective sedative for bronchoscopy. Patients in the remimazolam group reported higher satisfaction and faster cognitive recovery compared to those who received midazolam [39].

USE IN THE GERIATRIC POPULATION

The geriatric population is a growing group in society that undoubtedly requires special medical care and resources. Multimorbidity and the co-related polypharmacy increase the risk of adverse effects even with the use of drugs that are well established and relatively safe for the younger individuals. Accordingly, the elderly population may benefit most from a drug with low delirium potential, shorter duration of action and less depressant effects on the cardiovascular system. The described effects of remimazolam place it in a position worthy of consideration, particularly in the sedation and anesthesia of elderly patients.

The occurrence of delirium in patients is directly associated with a higher risk of complications, including deterioration in cognitive function [40], the onset of dementia [41] and the need for reoperation or rehospitalization or surgical complications [42].

Benzodiazepine use is considered one of the known risk factors for postoperative delirium. However, recent scientific evidence seems to contradict this common thesis. Regarding the incidence of delirium, use of remimazolam in elderly patients appears to be safe. Available studies did not show a statistically significant advantage of propofol over remimazolam when comparing the incidence of postoperative delirium after both drugs.

Remimazolam is a benzodiazepine and therefore has an antagonist, flumazenil, which reverses the effects of the drug, another important advantage in the prevention of postoperative delirium. The use of an antagonist can further reduce the risk of prolonged residual effects and sedation and thus reduce the risk of developing delirium. In a study by Kaneko *et al*. [43], a group of patients undergoing total intravenous general anesthesia with remimazolam who received flumazenil at the end of anesthesia had a lower rate of postoperative delirium compared with the propofol anesthesia group (8% vs. 26%; $P = 0.032$). More research is needed on this topic, especially comparing the proven and widely used midazolam with remimazolam. There are limited studies on the effects of reversing midazolam sedation with flumazenil on postoperative delirium. Available studies indicate that the use of flumazenil does not fully reverse the effects of midazolam sedation on cognitive abilities [44].

A notable advantage of remimazolam over propofol is the lower rate of induced intraoperative hypotension, which is a risk factor for postoperative delirium and postoperative cognitive decline [45]. In a study by Yang *et al*. [46], a statistically significant reduction in the number of hypotensive episodes defined as systolic blood pressure below 90 mmHg (17.1% vs. 43.0%; $P < 0.001$) and the need for pressor amines was observed during general anesthesia with remimazolam compared with the propofol group.

In addition, the elderly have a high prevalence of cardiovascular disease. As a result, reductions in blood pressure may be particularly harmful in this age group. Remimazolam has a lower risk of hypotension after induction of general anesthesia compared to propofol. A 2024 meta-analysis [47] based on 11 RCTs showed a lower incidence of post-induction and intraoperative hypotension (RR 0.41, 95% CI: 0.27–0.62, $P < 0.001$) and bradycardia (RR 0.58, 95% CI: 0.34–0.98, $P = 0.04$). Moreover, remimazolam is characterized by a lower incidence of hypoxemia during sedation and less pain at the injection site compared to propofol.

To ensure adequate hemodynamic stability, dosing should be appropriately tailored to the patient profile. Chae *et al*. [48] conducted a randomized study evaluating the effects of 6 remimazolam dose groups on patient parameters. Based on the results, the authors suggest bolus dose reductions for patients in older age groups: 0.19–0.25 mg kg^{-1} in the 60–80 years group and 0.14–0.19 mg kg^{-1} in the over 80 years group.

USE IN THE PEDIATRIC POPULATION

Remimazolam has been used in clinical practice for the past five years, but the majority of previous studies have focused on its use in adults. In contrast, its use in the pediatric population remains underresearched.

Available evidence suggests that the pharmacokinetics of remimazolam in the pediatric population is similar to that in adults. The drug is characterized by rapid clearance, a small volume of distribution, and a short context-sensitive half-life.

Approximately 50–70% of children undergoing surgery experience anxiety [49]. Benzodiazepines are a group of drugs that have demonstrated their usefulness in premedicating children for surgery. One advantage is that the drug can be administered without using the intravenous or intramuscular route, which is problematic in children. One of the routes of administration is the intranasal one, in which the usefulness of midazolam or a combination of midazolam and ketamine has been demonstrated [50, 51]. Moreover, remimazolam may be an effective option for the treatment of perioperative anxiety. A study by Long *et al*. [52] showed that intranasal administration of remimazolam is a safe and effective premedication option, with an ED_{95} (effective dose for 95% of the population) set by the authors at 1.57 mg kg^{-1} in young children and 1.09 mg kg^{-1} in preschool children, while a study by Ni *et al*. [53] showed a lower ED_{95} of only 0.78 mg kg^{-1} in preschool children for successful pre-induction sedation. A rare but problematic side effect of remimazolam use is a paradoxical reaction manifested as excessive agitation. The side effect that may be a limitation with intranasal use is nasal irritation, which may limit the child's cooperation [54].

Sedation in pediatric patients presents a unique set of challenges due to their physiological differences, heightened anxiety levels, and the need for rapid recovery with minimal side effects. Many procedures that do not require pharmacological preparation in adult patients require sedation due to the child's anxiety and impaired cooperation. A retrospective study by Hirano *et al*. [55] examined procedural sedation with remimazolam in 48 pediatric patients. The study noted that there was no fixed protocol for remimazolam dosing, with the drug administered using continuous intravenous infusion at a rate of 12 mg kg^{-1} h^{-1} until achieving the desired effect. After induction, the sedation depth was maintained within the range of 1–2 mg kg^{-1} h^{-1} at the anesthesiologist's discretion, with the use of additional pharmacological agents left to the anesthesiologist's choice. In the majority of cases (95%), remimazolam alone was insufficient for sedation. The median percent change from baseline to the lowest mean arterial pressure (MAP) was –22.6%. Notably, none of the patients required pharmacologic intervention for hemodynamic fluctuations. The cited study indicates that remimazolam might not provide sufficient sedation or analgesia when used as a single agent for certain pediatric procedures. Further research is necessary to assess the potential benefits of varying remimazolam dosages for sedation in pediatric patients, the efficacy of combining remimazolam with other anesthetics, and its application in specific procedures.

Remimazolam has been identified as a potentially valuable component of balanced general anesthesia. An observational study was conducted by Kimoto *et al*. [56] on a group of 418 children undergoing surgical procedures under general anesthesia. The intravenous induction dose of remimazolam used in the study was 12 mg kg^{-1} h^{-1}, administered until the desired effect was achieved. Subsequent infusions were administered at a rate of 1–2 mg kg^{-1} h^{-1}, accompanied by intermittent boluses of 0.2 mg kg^{-1}, with all dosing adjustments made ac-

cording to the anesthesiologist's clinical discretion. Other drugs used in balanced anesthesia included propofol, sevoflurane, fentanyl, remifentanil, morphine, and ketamine. Only 5% of children required ephedrine administration due to a drop in blood pressure, and 13.8% of the children developed PONV. Noteworthy was the short time for the return of consciousness. On average, the children met post-anesthesia care unit discharge criteria after 13.8 min.

The use of remimazolam at the end of surgery under general anesthesia for prevention of delirium in the pediatric population may also be a useful application. A randomized controlled trial by Yang *et al*. [57] demonstrated a significantly lower incidence of emergence delirium in the group receiving remimazolam 0.2 mg kg^{-1} compared with the group receiving a placebo (12% vs. 44%; RR 0.27, 95% CI: 0.12–0.60, $P < 0.001$) after tonsillectomy and adenoidectomy. The high incidence of delirium in the placebo group in this study may indirectly reduce the reliability of the results presented. In other available studies, the prevalence of delirium has been observed in the range of 1.3–25.5% in pediatric patients who underwent tonsillectomy/adenotonsillectomy procedures [58–60].

Pediatric patients with mitochondrial diseases are a group of patients who require special attention in the selection of an anesthetic agent. Many drugs commonly used in anesthesiology (propofol, inhaled anesthetics) are not applicable in these patients due to possible complications such as propofol infusion syndrome (PRIS) [61, 62]. Remimazolam may be a promising alternative. A case report by Yamadori *et al*. [63] indicated that remimazolam is safe in patients with MELAS (mitochondrial encephalopathy, lactic acidosis, and stroke-like episodes). In one patient with MELAS, remimazolam was used for an open gastrostomy. This case shows that it can be considered as an alternative to the previously popular midazolam, which has the disadvantage of a possible prolonged return of consciousness. Case reports suggest that remimazolam may also be an effective option in patients with muscular dystrophies such as Duchenne muscular dystrophy [64] and myotonic dystrophy [65, 66].

In rare conditions such as mitochondrial disorders or muscular dystrophies, the available information on remimazolam use comes from single cases. These preliminary findings are of very low certainty and should be viewed only as hypothesis-generating.

The potential long-term effects of remimazolam use in the pediatric population should also be considered. The developing body, particularly the central nervous system, may be more susceptible to potential toxic effects compared to the adult population. A study conducted by Zhou *et al*. [67] in mice showed that repeated administration of remimazolam caused behavioral changes and memory dysfunction by inducing neuronal apoptosis via glutamate excitotoxicity. Given the relatively short period of time that remimazolam has been in use, more time will be needed before studies analyzing the effects of remimazolam on remote neurological outcomes are available. Until then, caution should be exercised in the use of the drug, particularly in the pediatric population.

REMIMAZOLAM IN THE ICU

Current knowledge on the use of remimazolam for ICU sedation derives only from isolated case reports and pilot experiences. Such anecdotal data must be interpreted cautiously, as they cannot support generalized recommendations.

Although remimazolam has not yet been approved for sedation in the ICU within the European Union, it has already been studied for this indication in Asian countries such as Japan, South Korea, and China. However, most studies have involved a relatively small number of patients.

Chen *et al.* [68] investigated the use of remimazolam in a cohort of 23 ICU patients and demonstrated that its administration ensured hemodynamic and ventilatory stability in a group of postoperative patients. Similarly, Tang *et al.* [69] conducted a study in ICU patients requiring mechanical ventilation following non-cardiac surgical procedures. Remimazolam, at a dose of 0.125 to 0.15 mg kg^{-1} h^{-1}, provided mild to moderate sedation.

The same group further demonstrated, in a study involving 60 patients, that remimazolam induced a level of deep sedation comparable to propofol, as assessed using the Richmond Agitation and Sedation Scale (RASS) [70]. They found no significant differences between remimazolam and propofol regarding ventilation-free days, time to extubation, length of ICU stay, or 28-day mortality. Episodes of hypotension were observed in both groups, with no statistically significant difference in their incidence.

In a retrospective study analyzing adverse effects of remimazolam in a cohort of 6,806 patients, episodes of hypotension were reported in 1,006 patients (14.7%). In a direct comparison with propofol, the incidence of hypotension was lower with remimazolam (23% vs. 39%) [71]. These findings suggest that remimazolam may be a preferable option for sedation in hemodynamically unstable patients requiring vasopressor infusions.

Remimazolam shows potential for use in the treatment of status epilepticus in ICU patients, similar to midazolam [72]. Like midazolam, remima-

zolam provides rapid sedation and anticonvulsant effects. Its pharmacokinetic profile, characterized by rapid onset and metabolism independent of hepatic function, may offer advantages in critically ill patients, particularly those with organ dysfunction. Additionally, its predictable clearance and potential for reduced accumulation compared to midazolam could facilitate better titration and minimize prolonged sedation. Further studies are needed to confirm its efficacy and safety in managing refractory status epilepticus in the ICU setting.

Reports describing remimazolam in the treatment of status epilepticus are limited to individual patient descriptions. These observations are exploratory in nature and should not be considered as evidence sufficient to guide routine clinical practice.

SUMMARY

The introduction of remimazolam into anesthetic practice represents a significant advancement in the field of sedation and general anesthesia. Its ultra-short-acting nature, predictable pharmacokinetics, and minimal impact on hemodynamic stability offer a valuable alternative to traditional sedatives such as propofol, midazolam, and dexmedetomidine. However, despite its promising properties, several considerations must be made regarding its clinical application across different patient populations and procedural settings.

In conclusion, remimazolam offers clear recovery advantages when compared with midazolam, while in direct comparison with propofol, recovery times are generally similar. The main advantages of remimazolam over propofol lie instead in its favorable safety and hemodynamic profile, along with the availability of flumazenil as a reversal agent. These characteristics make remimazolam a valuable alternative in patients at risk of cardiovascular instability or prolonged benzodiazepine sedation, even though it does not shorten recovery relative to propofol.

Remimazolam provides certain advantages compared with conventional sedatives, notably greater hemodynamic stability, reduced pain on injection, and the availability of flumazenil as a reversal agent.

Compared to propofol, remimazolam demonstrates several clinically relevant advantages. It is associated with fewer cardiovascular adverse effects, such as hypotension and bradycardia, and a lower incidence of pain upon injection. Furthermore, its metabolism is largely organ-independent, making it a suitable option for patients with hepatic or renal impairment. Additionally, the availability of flumazenil as a reversal agent provides a safety net, allowing for rapid recovery from sedation if needed. This feature may be particularly beneficial in the prevention and management of postoperative delirium, especially in elderly patients.

When compared to dexmedetomidine, remimazolam provides a faster onset of sedation and fewer hemodynamic fluctuations. However, studies indicate that remimazolam may be associated with a higher risk of respiratory depression and oversedation. These findings suggest that while remimazolam is a useful alternative in cases where rapid sedation and recovery are priorities, careful monitoring of respiratory function remains necessary.

Remimazolam has been investigated for procedural sedation, general anesthesia, and ICU sedation. While the results are encouraging, challenges remain regarding dose optimization, cost-effectiveness, and limited evidence in rare clinical contexts.

Remimazolam has shown efficacy in a variety of settings, including procedural sedation, general anesthesia, and ICU sedation. In procedural sedation, it offers a favorable safety profile and rapid recovery times, making it an attractive alternative to midazolam and propofol. However, its slower onset of action (1–3 minutes) compared to propofol remains a limitation, particularly in short-duration procedures such as gastroduodenoscopy. Additionally, some studies have reported a high sedation failure rate in colonoscopy, suggesting that dose adjustments or combination regimens may be necessary to optimize its effectiveness in certain procedures.

In the ICU, remimazolam has demonstrated comparable sedative efficacy to propofol while maintaining hemodynamic stability, making it a promising option for critically ill patients, particularly those requiring vasopressor support. However, the current evidence is limited to small-scale studies, and further research is needed to establish its role in long-term ICU sedation.

Evidence for the use of remimazolam in special populations such as the elderly, pediatric patients, or those with mitochondrial or neuromuscular disorders remains scarce. Current data are based on small series or case reports, and further studies are required.

ELDERLY PATIENTS

The geriatric population may particularly benefit from remimazolam due to its rapid metabolism, lower risk of hypotension, and availability of a reversal agent. While benzodiazepines are traditionally associated with an increased risk of postoperative delirium, recent studies suggest that remimazolam does not significantly elevate this risk compared to propofol, especially when flumazenil is used. Nevertheless, caution should be exercised when administering remimazolam in elderly patients undergoing orthopedic procedures, as some trials have reported

a higher incidence of postoperative delirium in this subgroup.

PEDIATRIC PATIENTS

The use of remimazolam in pediatric anesthesia remains an area of ongoing research. Preliminary studies indicate that it may be an effective option for premedication and procedural sedation, particularly when administered intranasally. However, its role as a sole anesthetic agent in pediatric general anesthesia is not well established, with some studies reporting inadequate sedation when used alone. Future research should focus on determining optimal dosing regimens, assessing its long-term safety, and exploring its potential role in combination with other anesthetic agents.

FUTURE PERSPECTIVES AND RESEARCH DIRECTIONS

While remimazolam has demonstrated considerable potential, its widespread adoption requires further large-scale clinical trials to confirm its efficacy and safety across different patient populations and clinical scenarios. Specifically, future research should focus on:

- **Optimizing dosing strategies** for procedural sedation and general anesthesia, particularly in high-risk populations.
- **Comparative studies with propofol and dexmedetomidine** to further delineate its advantages and limitations.
- **Long-term safety assessments**, particularly in pediatric and elderly patients, to evaluate its impact on cognitive function and neurological outcomes.
- **Exploring novel applications**, such as its use in neuroanesthesia, awake sedation techniques, and sedation in patients with mitochondrial or neuromuscular disorders.

CONCLUSIONS

Remimazolam represents a significant advancement in anesthetic pharmacology, offering a safe and effective alternative to existing sedative agents. Its rapid onset, predictable metabolism, and favorable hemodynamic profile make it an attractive option in procedural sedation, ICU sedation, and general anesthesia. However, certain limitations, such as its slower onset in brief procedures and potential risk of oversedation, warrant further investigation. Continued research and clinical experience will ultimately determine its optimal role in anesthetic practice, ensuring that it is used to maximize patient safety and therapeutic efficacy.

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REFERENCES

1. Goudra BG, Singh PM. Remimazolam: the future of its sedative potential. Saudi J Anaesth 2014; 8: 388-391. DOI: https://doi.org/10.4103/1658-354X.136627.
2. Kilpatrick GJ, McIntyre MS, Cox RF, Stafford JA, Pacofsky GJ, Lovell GG, et al. CNS 7056: a novel ultra-short-acting benzodiazepine. Anesthesiology 2007; 107: 60-66. DOI: https://doi.org/10.1097/01.anes.0000267503.85085.c0.
3. Freyer N, Knöspel F, Damm G, Greuel S, Schneider C, Seehofer D, et al. Metabolism of remimazolam in primary human hepatocytes during continuous long-term infusion in a 3-D bioreactor system. Drug Des Devel Ther 2019; 13: 1033-1047. DOI: https://doi.org/10.2147/DDDT.S186759.
4. Antonik LJ, Goldwater DR, Kilpatrick GJ, Tilbrook GS, Borkett KM. A placebo- and midazolam-controlled phase I single ascending-dose study evaluating the safety, pharmacokinetics, and pharmacodynamics of remimazolam (CNS 7056): part I. Safety, efficacy, and basic pharmacokinetics. Anesth Analg 2012; 115: 274-283. DOI: https://doi.org/10.1213/ANE.0b013e31823f0c28.
5. Sheng XY, Liang Y, Yang XY, Li LE, Ye X, Zhao X, et al. Safety, pharmacokinetic and pharmacodynamic properties of single ascending dose and continuous infusion of remimazolam besylate in healthy Chinese volunteers. Eur J Clin Pharmacol 2020; 76: 383-391. DOI: https://doi.org/10.1007/s00228-019-02800-3.
6. Schüttler 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: 636-651. DOI: https://doi.org/10.1097/ALN.0000000000003103.
7. Zhou Y, Hu P, Jiang J. Metabolite characterization of a novel sedative drug, remimazolam in human plasma and urine using ultra high-performance liquid chromatography coupled with synapt high-definition mass spectrometry. J Pharm Biomed Anal 2017; 137: 78-83. DOI: https://doi.org/10.1016/j.jpba.2017.01.016.
8. Kilpatrick GJ. Remimazolam: non-clinical and clinical profile of a new sedative/anesthetic agent. Front Pharmacol 2021; 12: 690875. DOI: https://doi.org/10.3389/fphar.2021.690875.
9. Masui K. Remimazolam besilate, a benzodiazepine, has been approved for general anesthesia! J Anesth 2020; 34: 479-482. DOI: https://doi.org/10.1007/s00540-020-02755-1.
10. Wesolowski AM, Zaccagnino MP, Malapero RJ, Kaye AD, Urman RD. Remimazolam: pharmacologic considerations and clinical role in anesthesiology. Pharmacotherapy 2016; 36: 1021-1027. DOI: https://doi.org/10.1002/phar.1806.
11. Wiltshire HR, Kilpatrick GJ, Tilbrook GS, Borkett KM. A placebo- and midazolam-controlled phase I single ascending-dose study evaluating the safety, pharmacokinetics, and pharmacodynamics of remimazolam (CNS 7056): part II. Population pharmacokinetic and pharmacodynamic modeling and simulation. Anesth Analg 2012; 115: 284-296. DOI: https://doi.org/10.1213/ANE.0b013e318241f68a.
12. Chernik DA, Gillings D, Laine H, Hendler J, Silver JM, Davidson AB, et al. Validity and reliability of the Observer's Assessment of Alertness/Sedation Scale: study with intravenous midazolam. J Clin Psychopharmacol 1990; 10: 244-251.
13. Eisenried A, Schüttler J, Lerch M, Ihmsen H, Jeleazcov C. Pharmacokinetics and pharmacodynamics of remimazolam (CNS 7056) after continuous infusion in healthy male volunteers: part II. Pharmacodynamics of electroencephalogram effects. Anesthesiology 2020; 132: 652-666. DOI: https://doi.org/10.1097/ALN.0000000000003102.
14. European Medicines Agency. Byfavo: EPAR – Product Information 2024. Available at: https://www.ema.europa.eu/en/medicines/human/EPAR/byfavo.
15. Doi M, Morita K, Takeda J, Sakamoto A, Yamakage M, Suzuki T. Efficacy and safety of remimazolam versus propofol for general anesthesia: a multicenter, single-blind, randomized, parallel-group, phase IIb/III trial. J Anesth 2020; 34: 543-553. DOI: https://doi.org/10.1007/s00540-020-02788-6.
16. Wu Q, Xu F, Wang J, Jiang M. Comparison of remimazolam-flumazenil versus propofol for recovery from general anesthesia: a systematic review and meta-analysis. J Clin Med 2023; 12: 7316. DOI: https://doi.org/10.3390/jcm12237316.

17. Zhao TYM, Chen D, Xu ZX, Wang HL, Sun H. Comparison of bispectral index and patient state index as measures of sedation depth during surgeries using remimazolam tosilate. BMC Anesthesiol 2023; 23: 208. DOI: https://doi.org/10.1186/s12871-023-02172-3.
18. Wu X, Wang C, Gao H, Bai X, Zhang Z, Chen R, 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. DOI: https://doi.org/10.23736/S0375-9393.23.17034-9.
19. Chang Y, Huang YT, Chi KY, Huang YT. Remimazolam versus propofol for procedural sedation: a meta-analysis of randomized controlled trials. PeerJ 2023; 11: e15495. DOI: https://doi.org/10.7717/peerj.15495.
20. Zhao M, Hu H, Li X, Li X, Wang D, Kuang M. The safety and efficacy between remimazolam and propofol in intravenous anaesthesia of endoscopy operation: a systematic review and meta-analysis. Int J Surg 2023; 109: 3566-3577. DOI: https://doi.org/10.1097/JS9.0000000000000638.
21. Ko CC, Hung KC, Illias AM, Chiu CC, Yu CH, Lin CM. The use of remimazolam versus propofol for induction and maintenance of general anesthesia: A systematic review and meta-analysis. Front Pharmacol 2023; 14: 1101728. DOI: https://doi.org/10.3389/fphar.2023.1101728.
22. Zhang J, Cairen Z, Shi L, Pang S, Shao Y, Wang Y, et al. Remimazolam versus propofol for procedural sedation and anesthesia: a systemic review and meta-analysis. Minerva Anestesiol 2022; 88: 1035-1042. DOI: https://doi.org/10.23736/S0375-9393.22.16817-3.
23. Zhu X, Wang H, Yuan S, Li Y, Jia Y, Zhang Z, et al. Efficacy and safety of remimazolam in endoscopic sedation – a systematic review and meta-analysis. Front Med (Lausanne) 2021; 8: 655042. DOI: https://doi.org/10.3389/fmed.2021.655042.
24. Ri HS, Jeon S, Yeo J, Jung H, Kang C, Choo H. Efficacy of remimazolam in preventing postoperative nausea and vomiting: a systematic review and meta-analysis. Sci Rep 2025; 15: 29236. DOI: https://doi.org/10.1038/s41598-025-14976-z.
25. Mao Y, Guo J, Yuan J, Zhao E, Yang J. Quality of recovery after general anesthesia with remimazolam in patients' undergoing urologic surgery: a randomized controlled trial comparing remimazolam with propofol. Drug Des Devel Ther 2022; 16: 1199-1209. DOI: https://doi.org/10.2147/DDDT.S359496.
26. Yang JJ, Lei L, Qiu D, Chen S, Xing LK, Zhao JW. Effect of remimazolam on postoperative delirium in older adult patients undergoing orthopedic surgery: a prospective randomized controlled clinical trial. Drug Des Devel Ther 2023; 17: 143-153. DOI: https://doi.org/10.2147/DDDT.S392569.
27. Cai YH, Wang CY, Fang YB, Ma HY, Gao YQ, Wang Z. Preoperative anxiolytic and sedative effects of intranasal remimazolam and dexmedetomidine: a randomized controlled clinical study in children undergoing general surgeries. Drug Des Devel Ther 2024; 18: 1613-1625. DOI: https://doi.org/10.2147/DDDT.S461122.
28. Kurup MT, Sarkar S, Verma R, Bhatia R, Khanna P, Maitra S. Comparative evaluation of intraoperative dexmedetomidine versus lidocaine for reducing postoperative cognitive decline in the elderly: a prospective randomized controlled trial. Anaesthesiol Intensive Ther 2023; 55: 349-357. DOI: https://doi.org/10.5114/ait.2023.134251.
29. Lee S, Oh C, Jung J, Hong B, Jo Y, Lee S, et al. Retrospective comparison of the effects of remimazolam and dexmedetomidine on postoperative delirium in elderly patients undergoing orthopedic surgery of the lower extremities under spinal anesthesia. J Anesth 2024; 38: 771-779. DOI: https://doi.org/10.1007/s00540-024-03386-6.
30. 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: https://doi.org/10.2147/DDDT.S474854.
31. Rex DK, Bhandari R, Desta T, DeMicco MP, Schaeffer C, Etzkorn K, 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: 427-437.e6. DOI: https://doi.org/10.1016/j.gie.2018.04.2351.
32. Brzózka VM, Piotrowski AJ. Prospective, randomised comparison of two intravenous sedation methods for magnetic resonance imaging in children. Anaesthesiol Intensive Ther 2023; 55: 81-86. DOI: https://doi.org/10.5114/ait.2023.128715.
33. Abcejo AS, Teixeira MT. Remimazolam: patient safety considerations of a novel, practice-changing drug in perioperative medicine. APSF Newsletter 2023; 38: 80-83.
34. Chen S, Wang J, Xu X, Huang Y, Xue S, Wu A, et al. The efficacy and safety of remimazolam tosylate versus propofol in patients undergoing colonoscopy: a multicentered, randomized, positive-controlled, phase III clinical trial. Am J Transl Res 2020; 12: 4594-4603.
35. Chen SH, Yuan TM, Zhang J, Bai H, Tian M, Pan CX, et al. Remimazolam tosilate in upper gastrointestinal endoscopy: A multicenter, randomized, non-inferiority, phase III trial. J Gastroenterol Hepatol 2021; 36: 474-481. DOI: https://doi.org/10.1111/jgh.15188.
36. Zhang X, Li S, Liu J. Efficacy and safety of remimazolam besylate versus propofol during hysteroscopy: single-centre randomized controlled trial. BMC Anesthesiol 2021; 21: 156. DOI: https://doi.org/10.1186/s12871-021-01373-y.
37. Kim KM. Remimazolam: pharmacological characteristics and clinical applications in anesthesiology. Anesth Pain Med (Seoul) 2022; 17: 1-11. DOI: https://doi.org/10.17085/apm.21115.
38. Rex DK, Bhandari R, Lorch DG, Meyers M, Schippers F, Bernstein D. Safety and efficacy of remimazolam in high risk colonoscopy: a randomized trial. Dig Liver Dis 2021; 53: 94-101. DOI: https://doi.org/10.1016/j.dld.2020.10.039.
39. Kim S-H, Cho JY, Kim M, Chung JM, Yang J, Seong C, et al. Safety and efficacy of remimazolam compared with midazolam during bronchoscopy: a single-center, randomized controlled study. Sci Rep 2023; 13: 20498. DOI: https://doi.org/10.1038/s41598-023-47271-w.
40. Huang H, Li H, Zhang X, Shi G, Xu M, Ru X, et al. Association of postoperative delirium with cognitive outcomes: a meta-analysis. J Clin Anesth 2021; 75: 110496. DOI: https://doi.org/10.1016/j.jclinane.2021.110496.
41. Mohanty S, Gillio A, Lindroth H, Ortiz D, Holler E, Azar J, et al. Major surgery and long term cognitive outcomes: the effect of postoperative delirium on dementia in the year following discharge. J Surg Res 2022; 270: 327-334. DOI: https://doi.org/10.1016/j.jss.2021.08.043.
42. Meyer M, Götz J, Parik L, Renkawitz T, Grifka J, Maderbacher G, et al. Postoperative delirium is a risk factor for complications and poor outcome after total hip and knee arthroplasty. Acta Orthop 2021; 92: 695-700. DOI: https://doi.org/10.1080/17453674.2021.1980676.
43. Kaneko S, Morimoto T, Ichinomiya T, Murata H, Yoshitomi O, Hara T. Effect of remimazolam on the incidence of delirium after transcatheter aortic valve implantation under general anesthesia: a retrospective exploratory study. J Anesth 2023; 37: 210-218. DOI: https://doi.org/10.1007/s00540-022-03148-2.
44. Girdler NM, Fairbrother KJ, Lyne JP, Neave N, Scholey A, Hargaden N, et al. A randomised crossover trial of post-operative cognitive and psychomotor recovery from benzodiazepine sedation: effects of reversal with flumazenil over a prolonged recovery period. Br Dent J 2002; 192: 335-339. DOI: https://doi.org/10.1038/sj.bdj.4801369.
45. Kurup MT, Sarkar S, Verma R, Bhatia R, Khanna P, Maitra S, et al. Comparative evaluation of intraoperative dexmedetomidine versus lidocaine for reducing postoperative cognitive decline in the elderly: a prospective randomized controlled trial. Anaesthesiol Intensive Ther 2023; 55: 349-357. DOI: https://doi.org/10.5114/ait.2023.134251.
46. Yang JJ, Lei L, Qiu D, Chen S, Xing LK, Zhao JW, et al. Effect of remimazolam on postoperative delirium in older adult patients undergoing orthopedic surgery: a prospective randomized controlled clinical trial. Drug Des Devel Ther 2023; 17: 143-153. DOI: https://doi.org/10.2147/DDDT.S392569.
47. Pereira EM, Moraes VR, da Costa M, do Nascimento T, Slawka E, Galhardo Júnior C, et al. Remimazolam vs. propofol for general anaesthesia in elderly patients: a meta-analysis with trial sequential analysis. Eur J Anaesthesiol 2024; 41: 738-748. DOI: https://doi.org/10.1097/EJA.0000000000002042.
48. Chae D, Kim HC, Song Y, Choi YS, Han DW. Pharmacodynamic analysis of intravenous bolus remimazolam for loss of consciousness in patients undergoing general anaesthesia: a randomised, prospective, double-blind study. Br J Anaesth 2022; 129: 49-57. DOI: https://doi.org/10.1016/j.bja.2022.02.040.
49. Kassai B, Rabilloud M, Dantony E, Grousson S, Revol O, Malik S, et al. Introduction of a paediatric anaesthesia comic information leaflet reduced preoperative anxiety in children. Br J Anaesth 2016; 117: 95-102. DOI: https://doi.org/10.1093/bja/aew154.
50. Verma RK, Paswan A, De A, Gupta S. Premedication with midazolam nasal spray: an alternative to oral midazolam in children. Anesth Pain Med 2012 Spring; 1: 248-251. DOI: https://doi.org/10.5812/aapm.4567.
51. Bd V, Goyal S, Sharma A, Kothari N, Kaloria N, Sethi P, et al. Comparison of intranasal dexmedetomidine-midazolam, dexmedetomidine-ketamine, and midazolam-ketamine for premedication in paediatric patients: a double-blinded randomized trial. Anaesthesiol

Intensive Ther 2023; 55: 103-108. DOI: https://doi.org/10.5114/ait.2023.129276.
52. Long X, Wen LX, Yang H, Zhu GH, Zhang QY, Jiang JJ, et al. ED95 of remimazolam in nasal administration for attenuating preoperative anxiety in children. Front Med (Lausanne) 2023; 10: 1253738. DOI: https://doi.org/10.3389/fmed.2023.1253738.
53. Ni MJ, Jin YT, Wu QL, Zhang N, Tian JH, Li J, 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: https://doi.org/10.3389/fphar.2024.1372139.
54. Cai YH, Wang CY, Fang YB, Ma HY, Gao YQ, Wang Z, et al. Preoperative anxiolytic and sedative effects of intranasal remimazolam and dexmedetomidine: a randomized controlled clinical study in children undergoing general surgeries. Drug Des Devel Ther 2024; 18: 1613-1625. DOI: https://doi.org/10.2147/DDDT.S461122.
55. Hirano T, Kimoto Y, Kuratani N, Cavanaugh D, Mason KP. Remimazolam for pediatric procedural sedation: results of an institutional pilot program. J Clin Med 2023; 12: 5937. DOI: https://doi.org/10.3390/jcm12185937.
56. Kimoto Y, Hirano T, Kuratani N, Cavanaugh D, Mason KP. Remimazolam as an adjunct to general anesthesia in children: adverse events and outcomes in a large cohort of 418 cases. J Clin Med 2023; 12: 3930. DOI: https://doi.org/10.3390/jcm12123930.
57. 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: https://doi.org/10.2147/DDDT.S381611.
58. Liu K, Liu C, Ulualp SO. Prevalence of emergence delirium in children undergoing tonsillectomy and adenoidectomy. Anesthesiol Res Pract 2022; 2022: 1465999. DOI: https://doi.org/10.1155/2022/1465999.
59. Houben A, Ghamari S, Fischer A, Neumann C, Baehner T, Ellerkmann RK. Pediatric emergence delirium is linked to increased early postoperative negative behavior within two weeks after adenoidectomy: an observational study. Braz J Anesthesiol 2024; 74: 744114. DOI: https://doi.org/10.1016/j.bjane.2021.03.008.
60. Simonini A, Vittori A, Cascella M, Calevo MG, Marinangeli F. The impact of emergence delirium on hospital length of stay for children who underwent tonsillectomy/adenotonsillectomy: an observational retrospective study. Braz J Anesthesiol 2023; 73: 171-176. DOI: https://doi.org/10.1016/j.bjane.2021.10.006.
61. Shimizu J, Tabata T, Tsujita Y, Yamane T, Yamamoto Y, Tsukamoto T, et al. Propofol infusion syndrome complicated with mitochondrial myopathy, encephalopathy, lactic acidosis, and stroke-like episodes: a case report. Acute Med Surg 2020; 7: e473. DOI: https://doi.org/10.1002/ams2.473.
62. Finsterer J, Frank M. Propofol is mitochondrion-toxic and may unmask a mitochondrial disorder. J Child Neurol 2016; 31: 1489-1494. DOI: https://doi.org/10.1177/0883073816661458.
63. Yamadori Y, Yamagami Y, Matsumoto Y, Koizumi M, Nakamura A, Mizuta D, et al. General anesthesia with remimazolam for a pediatric patient with MELAS and recurrent epilepsy: a case report. JA Clin Rep 2022; 8: 75. DOI: https://doi.org/10.1186/s40981-022-00564-x.
64. Horikoshi Y, Kuratani N, Tateno K, Hoshijima H, Nakamura T, Mieda T, et al. Anesthetic management with remimazolam for a pediatric patient with Duchenne muscular dystrophy. Medicine 2021; 100: e28209. DOI: https://doi.org/10.1097/MD.0000000000028209.
65. Koyama Y, Nishikawa H, Murase Y, Morita K, Tsuzaki K. General anesthesia using remimazolam and remifentanil in combination with local anesthetics without neuromuscular blocking agents in a patient with myotonic dystrophy. Korean J Anesthesiol 2023; 76: 391-393. DOI: https://doi.org/10.4097/kja.23133.
66. Morimoto Y, Yoshimatsu A, Yoshimura M. Anesthetic management for a patient with myotonic dystrophy with remimazolam. JA Clin Rep 2021; 7: 10. DOI: https://doi.org/10.1186/s40981-021-00413-3.
67. Zhou XH, Zhang CC, Wang L, Jin SL. Remimazolam induced cognitive dysfunction in mice via glutamate excitotoxicity. Transl Neurosci 2022; 13: 104-115. DOI: https://doi.org/10.1515/tnsci-2022-0220.
68. Chen X, Zhang J, Yuan S, Huang H. Remimazolam besylate for the sedation of postoperative patients undergoing invasive mechanical ventilation in the ICU: a prospective dose–response study. Sci Rep 2022; 12: 19022. DOI: https://doi.org/10.1038/s41598-022-20946-6.
69. Tang Y, Yang X, Shu H, Yu Y, Xu J, Pan S, et al. Remimazolam besylate for sedation of postoperative patients in intensive care units: a phase I, open label, dose-finding study. Chin Med J (Engl) 2022; 135: 2134-2136. DOI: https://doi.org/10.1097/CM9.0000000000002243.
70. Tang Y, Gao X, Xu J, Ren L, Qi H, Li R, et al. Remimazolam besylate versus propofol for deep sedation in critically ill patients: a randomized pilot study. Crit Care 2023; 27: 474. DOI: https://doi.org/10.1186/s13054-023-04760-8.
71. Kempenaers S, Hansen TG, Van de Velde M. Remimazolam and serious adverse events. Eur J Anaesthesiol 2023; 40: 841-453. DOI: https://doi.org/10.1097/EJA.0000000000001902.
72. Hanley D, Pozo M. Treatment of status epilepticus with midazolam in the critical care setting. Int J Clin Pract 2000; 54: 30-35. DOI: https://doi.org/10.1111/j.1742-1241.2000.tb11838.x.