DOES AN EDUCATIONAL INTERVENTION ON THE BENEFITS OF REMIMAZOLAM FOR ENDOSCOPIC PROCEDURES CHANGE PRACTICE AND IMPROVE PATIENT OUTCOMES

Holly A. Nunn

A Project Report Submitted to
the Faculty of The School of Nursing at
The University of North Carolina at Greensboro
in Partial Fulfillment
of the Requirements for the
Doctorate in Nursing Practice

Greensboro
2024

Approved by:

Vadim Korogoda, DNP, CRNA	Project Team Leader
Wanda Williams, PHD, MSN, RN, WHNP-BC, CNE	DNP Program Director

Table of Contents

Dedication and Acknowledgements

I would like to dedicate this section to my support system throughout the process and completion of this project. A big thank you to my faculty advisor Dr. Korogoda for assisting me throughout this project to guarantee its completion and success. I am grateful for my anesthesia colleagues Anna Cornatzer, Michael Matthews, and Robert Mueller for their friendship, support, encouragement and assistance during this program and the course of this project.

I would like to give a special thank you to my mom for introducing me to the profession of anesthesia and for encouraging me to follow through with my childhood dream of becoming a nurse anesthetist. Thank you to my dad and two sisters, who along with my mom, supported me and prayed for me throughout this entire journey. Finally, I am especially appreciative of my husband, Hunter Nunn who never failed in showing me constant love, patience, and kindness, along with emotional and financial support. You provided a safe space for me to chase my dream and sacrificed endlessly along the way. I truly would not have been able to get through this anesthesia program or this project without you all!

Abstract

Background: Current anesthetics used for endoscopic procedures include primarily propofol, with or without midazolam or fentanyl. Common side effects of these frequently used medications include injection site pain, respiratory depression, hypotension, and prolonged return to baseline neurologic function. While these medications have been the standard, anesthesia techniques are constantly changing to improve patient outcomes. Recent studies have examined the use of remimazolam for sedation on patients undergoing endoscopic procedures such as endoscopy, colonoscopy, bronchoscopy, or transesophageal echocardiogram (TEE) to reduce adverse effects associated with currently utilized anesthetics for these procedures. **Purpose:** This DNP project intended to change practice and improve patient outcomes by utilizing current literature to educate anesthesia providers on the benefits of using remimazolam for endoscopic procedures in patients over the age of 65. **Methods:** This project used a pretest-posttest quantitative design with an additional survey component to address knowledge and barriers. An educational intervention was presented to anesthesia providers at the facility. Data collected and analyzed included pre and post intervention patient chart reviews, and post intervention anesthesia provider survey responses. **Results:** Provider use of remimazolam did not increase or decrease following the intervention, but overall patient outcomes were improved post-intervention. The survey found that anesthesia providers understood and agreed with the presented material and addressed barriers to implementation of the EBP recommendations presented. **Conclusion:** Findings support that an educational intervention for anesthesia providers on the use of remimazolam for endoscopic procedures in elder patients improves patient outcomes. Increased access to the anesthetic and additional follow up education is recommended to increase provider implementation of EBP recommendations of using remimazolam in the target population.

Keywords: remimazolam, sedation, anesthesia, endoscopic, colonoscopy, endoscopy, bronchoscopy, hemodynamic stability, hypotension, elderly, and safety.

Background and Significance

The practice of anesthesia is constantly evolving to enhance patient safety and satisfaction. The use of propofol and midazolam, with or without the addition of fentanyl, has been standard for endoscopic procedural sedation for some time; however, the side effects of these commonly used sedatives allow for a potentially better alternative drug to be found (Pastis et al., 2019). Common side effects of these frequently used medications include injection site pain, respiratory depression, hypotension, and prolonged return to baseline neurologic function. Patients often expect their surgical experience to present minimal discomfort. Consequently, patient comfort is an important part of anesthesia for surgical procedures and therefore prevention of injection site pain should be prioritized. Concerning hemodynamics, prolonged hypotension for as little as five minutes has the potential to induce detrimental effects of myocardial and/or renal injury (Ahuja et al., 2020). As well, while brief periods of apnea, and therefore hypoxia, are tolerated well in healthy patients, individuals who suffer from already compromised cardiopulmonary function have increased risks with transient anesthesia induced hypoxia (Bickler et al., 2017). Finally, lengthy sedation provoked neuropsychiatric depression may delay recovery and therefore increase PACU time, time to discharge, and elevate facility costs.

Remimazolam, an up and coming short acting benzodiazepine, may be a safe alternative to providing quality sedation without significant side effects such as hypotension, respiratory depression, pain on injection, or prolonged neuropsychiatric depression (Chen et al., 2020; Pastis et al., 2019). The mechanism of remimazolam is similar to that of midazolam in that it acts on GABA receptors in the brain to induce sedation, however unlike midazolam it is metabolized by plasma esterase which allows for rapid offset and neurologic recovery from the medication (Rex et al., 2018). With a considerable amount of anesthesia provided being to patients undergoing

endoscopic procedures, it is important to ensure the best possible anesthetic is being used for these procedures. The use of remimazolam for endoscopic surgeries has the potential to decrease intraoperative and postoperative hemodynamic compromise while providing adequate sedation for procedures and allowing for rapid recovery.

Purpose

The purpose of this Doctor of Nursing Practice (DNP) project is to observe the effect of an educational intervention delivered to practicing Certified Registered Nurse Anesthetists (CRNAs) and Anesthesiologists on evidence-based improved patient outcomes when using remimazolam on patients older than 65 for endoscopy, colonoscopy, transesophageal echocardiogram (TEE), or bronchoscopy procedures. Exclusive objectives are to evaluate the barriers to CRNA use of remimazolam, recognize and close knowledge gaps on current evidence-based literature on endoscopic patient problems and outcomes, and assess the efficiency of an educational intervention with a post-intervention knowledge survey and chart review of patient outcomes.

Review of Current Literature

A review of relevant literature was completed to evaluate current research on the benefits of using remimazolam for the sedation of patients over 65 years of age undergoing endoscopic procedures. The databases searched in this review included Cumulative Index to Nursing and Allied Health Lite (CINAHL), PubMed, Google Scholar, and Cochrane Library. The search contained the following keywords: *remimazolam, sedation, anesthesia, endoscopic, colonoscopy, endoscopy, bronchoscopy, hemodynamic stability, hypotension, elderly, and safety.* For articles examining remimazolam in endoscopic procedures inclusion criteria included systematic reviews, meta-analysis, and randomized control trials (RCTs) published in the English language between 2012 and 2022. Exclusion criteria for this topic included articles older than 2012, and

articles comparing the use of remimazolam for procedures other than colonoscopy, endoscopy, bronchoscopy, or transesophageal echocardiography (TEE). There were no publication date exclusion criteria when examining literature regarding other topics included in this review due to the significance of the original articles. The articles were reviewed, and the analysis included a total of 20 articles. A summary of the literature concluded that remimazolam is superior in providing hemodynamic stability and less pain on injection than currently used sedatives in anesthesia for endoscopic procedures.

Room for Growth

The practice of anesthesia is constantly evolving to improve patient safety, satisfaction, and outcomes. Sedation for endoscopic procedures was historically done using primarily benzodiazepines and narcotics. This was until propofol was introduced and became more popular due to its pharmacokinetic properties of rapid on/offset and predictable recovery process (Lin, 2017). Although still effective, the side effects of these commonly used sedatives allow for a better alternative medication to be found (Pastis et al., 2019). Anesthesia providers deliver anesthetics for a large volume of outpatient surgeries daily, therefore it is important to ensure the best possible anesthetic is being used for patients undergoing these procedures. Use of remimazolam for outpatient procedural sedation surgeries has the been shown to decrease intraoperative and postoperative hemodynamic compromise while providing adequate sedation for procedures and allowing for rapid recovery.

Remimazolam

The mechanism of remimazolam is similar to that of midazolam in that it acts on GABA receptors in the brain to induce sedation. However unlike midazolam, it is metabolized by plasma esterase, which allows for rapid offset and neurologic recovery from the drug (Rex et al.,

2018). In comparison to commonly used sedatives such as midazolam, propofol, and etomidate, remimazolam offers comparable sedation levels. However, literature suggests this medication achieves a higher safety profile for endoscopic procedures (Zhu et al., 2021). An article by Kim and Fechner discuss that short- and long-term side effects of remimazolam have yet to be discovered, but further investigation is warranted on its effects on postoperative nausea and vomiting (PONV), cancer metastasis, and incidence of postoperative cognitive decline (POCD) (2022). Overall, remimazolam has been shown to produce effective sedation while maintaining blood pressure, oxygen saturation, and reducing injection pain. Several studies have determined that remimazolam maintains hemodynamics during sedation and is a safe sedative to use (Pastis et al., 2019; Rex et al., 2021; Zhu et al., 2021).

Sedation Adequacy

The sedation efficacy of remimazolam is important to evaluate first. This trait of the drug determines whether it is suitable for providing adequate amnesia and anesthesia for procedural sedation. Research indicates that remimazolam induces sedation quickly. Rapid induction of sedation is extremely beneficial in outpatient surgeries and for procedural sedation (Antonik et al., 2012; Rex et al., 2021). Other important aspects of assessing adequacy of anesthesia include patient and surgeon satisfaction. Therefore, it is significant that the use of remimazolam produces at least similar patient and provider satisfaction scores as the use of propofol-etomidate in a study comparing the use of these sedatives for colonoscopy, a common outpatient procedure (X. Liu et al., 2021).

Another consideration of anesthetic virtue is the procedural success rate. Success is deemed if the provider is able to complete the procedure. Remimazolam had a success rate of 96.5% and 96.9%, but fell slightly short to propofol at 100% in two studies in regard to

continuous sedation (Chen et al., 2020; X. Liu et al., 2021). However, higher initial doses of remimazolam proved to be comparable to propofol for induction of anesthesia, and it was determined that there was no significant difference in induction success rate between these two drugs (Dai et al., 2021). A comparison of remimazolam to propofol is found in several studies because propofol is currently widely used for procedural sedation. Nevertheless, the drugs' comparison to midazolam is just as significant, as this drug is also used for a large majority of outpatient surgeries. Remimazolam produces amnesia in similar fashion to midazolam, but it induces effects more quickly, resulting in a deeper level of amnesia (Antonik et al., 2012; Rex et al., 2018). Furthermore, the procedural success rate with the use of remimazolam verses midazolam was significantly superior, indicating that remimazolam produces much more efficient sedation than midazolam (Jhuang et al., 2021). When compared to midazolam, remimazolam offers similar to superior sedation while patient hemodynamics have minimal variation when comparing the two. Ul-Haque et al. even suggests that remimazolam could potentially take the place of midazolam for procedural sedation in the future (2022).

A systematic analysis of seven relevant studies concluded that remimazolam has a higher sedative efficacy than midazolam, but slightly lower than propofol (Zhu et al., 2021). Although the sedation level produced by remimazolam falls slightly short to propofol, the benefits of its use outweigh the small risk (< 4%) of not achieving procedural success. It must finally be considered that remimazolam, as one study stated stated, "still achieved its primary endpoint of procedural sedation" (Pastis et al., 2019, p. 143).

Hemodynamic Stability

Hypotension

One of the most significant adverse effects regarding hemodynamic stability during

sedation is the rate with which an anesthetic agent compromises cardiovascular function, measured by hypotension. Propofol is one of the most widely used anesthetics used for procedural sedation. It has proven to cause intraoperative hypotension for endoscopic procedures, especially colonoscopy. (Sneyd et al., 2022)

There are many studies that evaluate the relationship of intraoperative hypotension to severe incidents such as myocardial infarction, acute kidney injury, and stroke. A systematic review found that exposure to mean arterial pressure (MAP) <80 mmHg for ≥10 minutes, or MAP <70 mmHg for even lesser time was linked to somewhat elevated risk for organ damage. Additionally, patients subject to a few minutes of MAP <60-65 mmHg or any exposure to MAP <50-55 mmHg had a high risk of end organ damage. (Wesselink et al., 2018)

Although some patients can tolerate a transient decrease in blood pressure, this can be a detrimental adverse effect in elderly patients and those with low cardiac reserve. Many patients coming in for endoscopic procedures are often elderly patients with comorbidities, and present in a dehydrated state due to bowel prep or NPO status. This puts these patients at even higher risk of experiencing intraoperative hypotension. (Sneyd et al., 2022) Multiple studies from their research concluded that remimazolam had a significantly lower rate of hypotension when compared to propofol and midazolam (Chen et al., 2020; Dai et al., 2021; Rex et al., 2018; Ul-Haque et al., 2022; Zhu et al., 2021). Therefore, remimazolam asserts its appeal by lessening rates of intraoperative hypotension and decreasing the patient's risk of experiencing the aforementioned effects.

Respiratory Depression

Sedation for endoscopic procedures has typically involved the technique of monitored anesthesia care (MAC), where patients are asleep without needing an endotracheal tube or

mechanical ventilation. The detriment to this practice is the amplified opportunity for respiratory depression, apnea, and hypoxia in these patients. Heuss and Inauen affirm that propofol has a narrow therapeutic range which increases the risk of unintentional deep sedation when used for endoscopic procedures. This concurrently impairs spontaneous ventilation leading to prolonged periods of apnea, and therefore hypoxia (Heuss & Inauen, 2004). Opioids are also commonly used in conjunction with propofol for endoscopic sedation. An article by Montadon and Slutsky addresses opioid induced respiratory depression. Opoids, while providing pain relief, also inhibit two cortical areas critical to breathing regulation. This effect can provoke hypoventilation characterized by decreased respiratory rate, diminished airflow, apnea, and severe hypoxemia (Montandon & Slutsky, 2019).

Significant implications such as myocardial infarction, ischemic brain injury, and neurocognitive decline are possible outcomes of prolonged hypoxia in healthy patients. These detrimental effects can occur even with transient hypoxia in patients with pre-existing cardiovascular and/or pulmonary disease (Bickler et al., 2017). Research indicated that the incidence of hypoxia had a lesser differential between remimazolam, propofol, and midazolam and was not as significant as hypotension. However, results of the systematic review of seven studies regarding the efficacy and safety of remimazolam confirmed that the incidence of hypoxia, defined at respiratory rate <8 breaths/min and/or oxygen saturation <90%, was still considerably less with the use of remimazolam versus propofol. (Zhu et al., 2021) Another recent systematic review and meta-analysis of nine studies comparing remimazolam and propofol for procedural sedation and general anesthesia also reiterated that the incidence of hypoxemia in remimazolam was significantly less than with propofol (Zhang et al., 2022).

Pain on Injection

Jalota et al. noted that discomfort at injection site is an adverse effect of propofol. This systematic review and meta-analysis reported that about three out of five patients have pain on injection with propofol. One out of five actually described the pain to be excruciating, and deemed induction with propofol to be the "most painful part of the perioperative period" (Jalota et al., 2011). A study by Dai et al. revealed that the rate of pain on injection was at a high of 27% for propofol (2021). Patients experiencing pain causing an increase in heart rate and blood pressure. Sedation could be delayed due to the need to slow the injection rate to reduce the pain on injection (Jalota et al., 2011). Additionally, burning can potentially cause the patient to have decreased satisfaction, and as Medicare is transitioning on reimbursement based on patient satisfaction could lead to decreased hospital income (L. Liu et al., 2021). Significantly, multiple studies note that remimazolam does not produce pain at injection site, whereas propofol has a substantial incidence rate (Antonik et al., 2012; Chen et al., 2020; Dai et al., 2021; Guo et al., 2022; X. Liu et al., 2021; Rex et al., 2018; Zhang et al., 2022; Zhu et al., 2021).

Neurologic Recovery

Midazolam, a benzodiazepine allosterically increasing GABA activity, remains a commonly used medication for procedural sedation (X. Liu et al., 2021). X. Liu et al. states in his study that this medication's extended elimination half-life (1.8-6.4 hours) prolongs post-procedure sedation due to the lengthy circulation of its active metabolite (2021). A study by Antonik et al. found that midazolam has a mean residence time seven times that of remimazolam (2012). This prolonged residence time is problematic, especially in the elderly population over 70 years of age. The lengthy offset of sedation effects results in lingering drowsiness and slower return of complete neuropsychiatric function for patients receiving midazolam as part of their

sedation.

Due to the plasma esterase metabolism of remimazolam, patients can rapidly recover from sedation. Remimazolam promotes a full return of cognitive function within minutes (Rex et al., 2021). This full return of normal cognitive function is significant in that patients are not left with lingering drowsiness, and clarity of thought returns to baseline after their procedure is complete (Kim & Fechner, 2022). This trait of remimazolam allows for safer patient conditions at discharge. In a study comparing propofol-etomidate sedation to remimazolam, it was found that time to fully alert, time to be ready for discharge, and time to actual hospital discharge was considerably lower in patients receiving remimazolam (X. Liu et al., 2021).

Another benefit of remimazolam is that its metabolic process allows for a low context sensitive half-time, meaning that rapid recovery occurs even when using higher doses/quantity of the drug to achieve sedation (Antonik et al., 2012). This low context sensitive half time is significant as it provides reassurance for anesthetists using remimazolam, that higher doses can be given to provide successful sedation without delayed patient recovery or hindered operating room turnover. Remimazolam also offers the benefit of rapid induction of sedation, while maintaining the important benefit of extremely quick offset allowing for rapid return of normal neurologic functioning (X. Liu et al., 2021). This advantage is important for post-operative patient safety as well as decreased time to discharge, and patient safety following discharge.

A Better Anesthetic

Anesthesia providers have the responsibility of providing the safest possible care for patients during surgery, thus patient hemodynamic stability is a top priority. Along with patient safety, patient satisfaction is also an important part of the anesthesia providers responsibility. Currently used anesthetics discussed above are effective in achieving sedation but risk

detrimental side effects that can increase patient morbidity and mortality (Antonik et al., 2012; Heuss & Inauen, 2004; Montandon & Slutsky, 2019; Sneyd et al., 2022). Remimazolam, an up and coming short acting benzodiazepine, is a safe alternative to providing quality sedation without significant side effects such as hypotension, respiratory depression, pain on injection, or prolonged neuropsychiatric depression (Chen et al., 2020; Pastis et al., 2019). Therefore, it can be concluded that remimazolam is a superior choice for sedation in these procedures.

Methods

Design

This DNP project utilized a pretest-posttest quantitative design with an additional survey component to address knowledge and barriers. The goal of this project was quality improvement. The project took place at a local community hospital in western North Carolina. Flyers were posted at the facility and regarding date and time of the educational intervention. Quantitative data was utilized and compared from a retrospective chart review two weeks before, and two weeks after the educational intervention to assess patient outcomes. Quantitative data from a post-intervention paper survey was also used to address barriers to change in practice. The post-intervention survey was distributed to participating anesthesia providers two weeks following the educational intervention to assess practice change, perceived patient outcomes, and barriers. Primary outcomes of this project include adaptation of remimazolam use for endoscopic procedures particularly in the elderly population, patient intraoperative hemodynamic stability (blood pressure, oxygen saturation, respiratory rate), and incidence of pain on injection. Secondary outcomes include change in knowledge among anesthesia providers after the educational intervention, time to PACU discharge, and perceived barriers to use of remimazolam for endoscopic procedures.

Evidence Based Practice Model

The IOWA Model of Research-Based Practice to Promote Quality Care was used to conduct this DNP project. This EBP model was developed to encourage and assist health care providers in implementing current research discoveries to improve quality of patient care (Titler et al., 2001). The PI identified priorities in the practice of endoscopic anesthesia including patient safety and hemodynamic stability (blood pressure, respiratory rate, oxygen saturation, injection pain, and neurologic recovery). Review of current literature suggested implementation of a change in practice may be beneficial to patients undergoing endoscopic anesthesia.

This model was chosen with intentions to base this project on knowledge focused triggers, specifically a knowledge deficit about new literature that indicates remimazolam may be a superior anesthetic choice for patients over age 65 undergoing endoscopic procedures. The facility at which this project was implemented performs a large quantity of endoscopic procedures on the proposed targeted patient population (age 65+). This indicated that this topic is a priority for this organization, fulfilling the next step of the IOWA model. The PI reviewed current literature on remimazolam and synthesized the data. A final step in the IOWA model before any implementation is determination of sufficient research. The data accumulated and synthesized assessed and determined there was adequate evidence to suggest that remimazolam could be a better anesthetic choice and improve patient outcomes. Education of certified registered nurse anesthetists (CRNAs) and anesthesiologists on the data achieved from the literature review serves as piloting the change in practice. This was in effort to increase use of remimazolam and improve outcomes in the targeted patient population. Chart review of patient outcomes were compared to post-educational intervention patient outcomes and anesthesia providers post-assessment survey addressing barriers. If the intervention is successful in

improving knowledge of this drug, therefore increasing the use of remimazolam and improving patient outcomes, this change may be beneficial to institute into the daily practice of endoscopic anesthesia. This would then complete the final step of the IOWA model.

Theoretical Framework

This DNP project utilize Lewin's Three-Step Model for Change as the framework. According to Kurt Lewin (1951) individuals and groups are influenced by restraining forces which maintain complacency and driving forces which encourage change. His model focuses on *unfreezing, changing (or transitioning),* and *refreezing* being the three stages of implementing change (Lewin, 1951; Shirey, 2013). A problem and proposed solution has been identified through this project. The PIs goal was to encourage change in the practice of endoscopic anesthesia by educating anesthesia providers on the research-based findings that use of remimazolam improves patient outcomes.

The first step in Lewin's change model is *unfreezing* and focuses on preparation for change. This stage places emphasis on recognizing and understanding the necessity for change in practice (Shirey, 2013). The problem of hemodynamic instability during anesthesia for endoscopic procedures on elderly patients has indicated a need for change. This project served to decrease the restraining force of lack of knowledge about a better anesthetic for these procedures. The goal of this project was to encourage the driving force for positive change by detecting barriers to changing endoscopic anesthesia techniques and enhancing knowledge on remimazolam.

Establishment of a plan of action occurs during the *transitional* phase, the second stage of Lewin's theory. This step involves coaching individuals to overcome resistance to change and increasing the driving force above restraining forces (Shirey, 2013). Implementation of this

project included an educational intervention of current literature provided to CRNAs and anesthesiologists who deliver endoscopic anesthesia. Education emphasized and proposed a solution to hemodynamic instability, neurologic recovery, and discomfort during sedation for endoscopic procedures. This intervention hoped to aid anesthesia providers with understanding the problem and formulating a plan to improve patient outcomes who undergo endoscopic procedures.

Refreezing is what Lewin uses to describe the last phase of stabilizing change and adapting it into current practice (1951; Shirey, 2013). Chart reviews assessed the usage of remimazolam and patient outcomes two weeks after the intervention. Post-intervention surveys were used to evaluate barriers to CRNAs implementing change. This allows providers to address and eliminate the understood obstacles to promote future sustained practice change.

Permissions

The PI received verbal and written permission from the chief of anesthesia and CRNA clinical director at the facility. The anesthesia departments clinical coordinator assisted as the point of contact and advisor for the implementation of this project. The PI obtained approval from the UNCG and facility Institutional Review Board before implementing this project.

Setting and Sample

This project took place at a local community hospital in western North Carolina with 117 inpatient beds, 10 operating rooms, and two endoscopy suites. The participants for this project included anesthesia providers who practice endoscopic anesthesia. Convenience sampling was used to recruit participants. Inclusion criteria for participants was currently practicing Certified Registered Nurse Anesthetists (CRNAs) and anesthesiologists at the facility who deliver anesthesia to patients undergoing endoscopic procedures. The exclusion criteria was SRNAs or

non-CRNAs, and CRNAs or anesthesiologists who do not provide anesthesia for endoscopic procedures. The target participant goal was 24 anesthesia providers, which is the total number of practicing CRNAs and anesthesiologists at this facility.

Implementation

A recruitment flyer with the date, time, location, and topic of the educational intervention was posted in the anesthesia break room, chief CRNA's office, and anesthesia meeting room to distribute information about the project. Participation was voluntary, and informed consent was implied by participation in the educational intervention and completion of the two-week post-intervention survey. An educational intervention describing the benefits of using remimazolam for sedation for endoscopic procedures was presented to anesthesia providers before a morning anesthesia staff meeting. A post-intervention survey was distributed to participating anesthesia providers two weeks following the educational intervention to assess practice change, perceived patient outcomes, and barriers. Additionally, a chart review two weeks pre and post intervention was done to assess patient outcomes.

Instruments

A post intervention survey was developed by the PI and included multiple choice, Likert-scaled questions. The multiple-choice questions assessed gender, participant's length of practice, and frequency providing anesthesia for endoscopic procedures in the past 30 days. Likert-scaled questions were used to assess CRNA perceived incidence of pain on injection, hypotension, respiratory depression, hypoxia, and neurologic recovery. Likert-scaled questions were also used to assess providers use of remimazolam and identify barriers to implementing change in practice. One open-ended question was included to give the participant an opportunity to add any perceived barriers not mentioned in the Likert-scaled questions.

Data Collection

The PI performed a pre and post intervention chart review two weeks prior to and following the educational session. For this chart review the PI recorded the last 80 eligible patient charts. Inclusion criteria for charts reviewed included patients who underwent colonoscopy, endoscopy, or bronchoscopy, patients over the age of 65, and patients who received either propofol or remimazolam as their primary anesthetic. Exclusion criteria for chart review included patients who received any sedatives/hypnotics other than propofol, remimazolam, midazolam, or fentanyl, and patients who received a combination of remimazolam and propofol.

The recorded chart data included day of surgery, age, ASA score, procedure type, primary anesthetic (propofol or remimazolam), intraoperative hemodynamics, and time to post anesthesia care unit (PACU) discharge. Hemodynamic data included number of hypotensive blood pressures from start to end of procedure. Hypotension was defined as any blood pressure less than 20% of patients first in room blood pressure before the procedure began. Hemodynamic data also included respiratory depression defined as respiratory rate less than 8 breaths per minute, and hypoxia defined as any oxygen saturation recorded below 90%. Time to PACU discharge was calculated from the time the patient entered the recovery room, to the time the patient left the recovery room. No patient identifiers were collected. All data was recorded using Microsoft Excel.

Post-intervention surveys were placed in the chief nurse anesthetist's office two weeks after the educational intervention and participants were notified by the chief anesthetist where surveys were located. Envelopes to seal the surveys and a collection box were left in the chief anesthetist's office to collect surveys.

Data Analysis

Chart review data of patient charts were analyzed using Microsoft excel data analysis tool pack with the guidance of a statistician faculty member at the UNCG School of Nursing. Pre-intervention chart review results were compared to post-intervention chart review results to determine the rate of use of remimazolam for endoscopic procedures. Post-intervention chart reviews were compared to pre-intervention chart reviews to assess the difference in rates of hypotension, respiratory depression, hypoxia, and time to PACU discharge for patients after the educational intervention. Descriptive statistics were used to analyze survey data. Descriptive statistics were also utilized to discuss pre and post intervention chart review result data.

Budget, Time, and Resources

No financial resources were required for this project. The educational intervention took 20 minutes and the post-intervention survey took approximately 5 minutes to complete. The PI provided light breakfast snacks and coffee for the participants the day of the educational intervention.

Results

Chart Reviews

Pre and post intervention chart reviews of a total of 160 patients who met inclusion criteria revealed that overall 68.7 % of patients who received propofol for sedation experienced hypotension versus only 30% of patients who received remimazolam. Hypotensive episodes were defined as any blood pressure lower than 20% of the patient's pre-sedation baseline blood pressure. In the pre-intervention data the average number of hypotensive episodes for patients who received remimazolam was 0.6 episodes per case. The highest number of hypotensive episodes in a case that used remimazolam for sedation was 1 episode of hypotension. The

average number of hypotensive episodes during a case for patients who received propofol for sedation was 3.41. The most hypotensive episodes during a case in which propofol was used was 10. Post-intervention chart reviews revealed that the average number of hypotensive episodes when using remimazolam was 0. This result was again lower than the average number of hypotensive episodes when using propofol, which was 2.04. The highest number of hypotensive episodes for remimazolam was 0 and propofol was 8.

Differences in respiratory depression and hypoxia rates were less significant. Respiratory depression was defined as any respiratory rate less than 8 breaths per minute and hypoxia was defined as any oxygen saturation less than 90% for any period of time. Two patients from the pre-intervention chart review experienced respiratory depression and both received propofol for sedation. No patients from the post-intervention chart review experienced respiratory depression. One patient that received propofol from the pre-intervention chart review had a hypoxic episode, while zero patients experienced hypoxia in the post-intervention chart review.

Pre-intervention chart reviews displayed patients who received remimazolam for sedation had an average post anesthesia care unit (PACU) discharge time of 32 minutes with a minimum time of 24 minutes and maximum time of 38 minutes. Patients who received propofol had an average PACU discharge time of 21.6 minutes with a minimum of 9 minutes and a maximum of 62 minutes. Post-intervention chart reviews showed patients sedated with remimazolam had an average post anesthesia care unit (PACU) discharge time of 27.8 minutes with a minimum time of 18 minutes and maximum time of 40 minutes. Patients who received propofol had an average PACU discharge time of 26.1 minutes with a minimum of 10 minutes and a maximum of 128 minutes. The overall average time to PACU discharge of 160 patient chart reviews for propofol was 23.9 minutes, while remimazolam was 29.9 minutes.

Anesthesia provider utilization of remimazolam for endoscopic procedures in patients over the age of 65 was the same pre and post intervention. However, overall rates of hypotension were significantly decreased ($P < 0.00045$) post intervention. Pre intervention chart reviews of all 80 patients receiving sedation for included endoscopic procedures displayed an overall average of 3.24 hypotensive BP readings. Post intervention chart reviews of all 80 patients receiving sedation for included endoscopic procedures revealed a decreased overall average of 1.91 hypotensive BP readings.

Post Intervention Survey

A total of 20 anesthesia providers participated in the educational intervention, of which 19 responded via the post-intervention survey, with a gender distribution of 42.1% male (8) and 57.9% female (11). When asked about their years of experience as an anesthesia provider the majority fell into the category of > 15 years of experience, with 10 individuals, followed by 9 who had 5-15 years of experience. None of the respondents had less than 5 years of experience in this role. This suggests an experienced group of anesthesia providers. In terms of the frequency of practicing anesthesia for endoscopic procedures in the last month, 1 (5.3%) reported daily practice, 12 (63.2%) practiced 2-3 times per week, 5 (26.3%) practiced 2-3 times per month, and 1 (5.3%) never practiced anesthesia for these procedures. Therefore majority of providers who participated in the educational intervention and post educational survey provide anesthesia for the target patient population.

When providers were asked about the incorporation of remimazolam into their practice for patients undergoing colonoscopy, endoscopy, bronchoscopy, or TEE, 4 (21.1%) reported never using remimazolam, 2 (10.5%) used it rarely, 9 (47.4%) used it occasionally, 3 (15.8%) used it frequently, and 1 (5.3%) used it very frequently.

Perceptions

Participants were asked about the perceived impact of remimazolam compared to propofol in terms of hypotension, respiratory depression, hypoxia, pain on injection, and prolonged neurologic recovery to assess post-educational intervention knowledge. In response to these questions, 19 anesthesia providers reported their perceptions. For hypotension, 8 (42.1%) agreed, and 11 (57.9%) strongly agreed that remimazolam is effective in decreasing the incidence of hypotension compared to propofol. Regarding respiratory depression, 7 (36.8%) agreed, and 12 (63.2%) strongly agreed with the effectiveness of remimazolam minimizing these events. For hypoxia, 8 (42.1%) agreed, 1 (5.3%) neither agreed nor disagreed, and 10 (52.6%) strongly agreed. In terms of pain on injection, 7 (36.8%) agreed, and 11 (57.9%) strongly agreed that remimazolam has minimal to none. Lastly, for prolonged neurologic recovery, 6 (31.6%) agreed, and 7 (36.8%) strongly agreed that remimazolam is superior to propofol regarding speed of neurologic recovery.

Barriers

Barriers to utilization of remimazolam for endoscopic procedures were assessed on the post-intervention survey. Pre-written survey questions were provided along with the option for providers to add free-text responses to address any barriers that were not mentioned. The top barrier reported was agreed upon by 12 (63.2%) providers that remimazolam is not as readily available as other anesthetics. Respondents also had an opportunity to add any barriers that were not a part of the Likert scale provided. One provider elaborated by stating “not stocked in Pyxis/Omnicell all the time/at all locations”. Another reported that they “forget it is an option”, possibly being related to remimazolam not being as available as other anesthetics. The second leading barrier was reported by 10 (52.6%) that remimazolam costs more than other primary

anesthetic choices. This was followed by two (10.5%) provider reports of the reconstitution of remimazolam being a barrier. Finally, one (5.2%) respondent selected that they are not comfortable using a less familiar anesthetic when providing sedation for patients undergoing endoscopic procedures, and one (5.2%) reported they would like to see more evidence-based support in the literature to integrate the presented interventions into their practice. One provider also added a barrier that "new providers may not be familiar with the dosing/use" of remimazolam. Two providers indicated that they do not feel remimazolam provides adequate sedation for endoscopic procedures. Their responses included "it does not get some patients deep enough and end up having to give propofol anyways" and "I am not confident in using it as the sole anesthetic agent for stimulating procedures such as EGD".

The final post-intervention survey question asked if providers will use/continue to use remimazolam for sedation in fragile patients undergoing endoscopic procedures. Seventeen (89.5%) respondents reported that they plan to utilize remimazolam in their practice.

Discussion

Findings of this project revealed anesthesia provider practice preferences, knowledge, and challenges regarding the use of remimazolam for elder patients undergoing endoscopic procedures. All participating providers agreed that remimazolam does decrease the rates of hypotension and respiratory depression compared to propofol. All but one provider agreed that remimazolam also has less pain on injection than propofol, and majority of providers agreed remimazolam decreases incidence of hypoxia and increases speed of neurologic recovery compared to propofol. This indicates that participants agree with the literature that remimazolam is a safe sedative without significant side effects such as hypotension, respiratory depression, pain on injection, or prolonged neuropsychiatric depression (Chen et al., 2020; Pastis et al., 2019). Therefore providers seem to be aware of the benefits of remimazolam use in patients

older than 65 undergoing anesthesia for endoscopic procedures and its ability to improve patient safety and outcomes. The provider perception survey responses display that there is minimal knowledge gap between anesthesia providers understanding and the literature on the benefits of remimazolam. Therefore the barriers to increasing utilization of remimazolam for endoscopic procedures in patients over the age of 65 must provide some rationale for no increase in use of remimazolam following the educational intervention.

Participants displayed an understanding of the education presented, yet the utilization of remimazolam did not increase nor decrease. This could be due to providers who already integrated remimazolam into their practice continuing to use remimazolam, but reserving its use for frail patients who would benefit most from increased hemodynamic stability. Assessment of barriers to using remimazolam sought to understand and address the lack of increase in utilization. The leading barrier reported was that remimazolam was not as readily available as other anesthetics. Several free text responses also coincided with this barrier, stating remimazolam is not always stocked in the medication dispenser that providers use for endoscopic procedures. This barrier can be addressed with the facilities anesthesia leaders in effort to increase the opportunities for providers to use remimazolam. Other barriers included increased cost, the need to reconstitute, unfamiliar with the sedative, and desire for more evidence-based literature before using. These barriers can also be addressed by the facility by providing additional education. Two providers included in their free text a barrier that was not initially addressed in the survey. They stated they did not feel remimazolam alone provided enough sedation for these procedures. Literature acknowledges that remimazolam falls slightly (< 4 %) short to propofol regarding sedation efficacy (Chen et al., 2020; X. Liu et al., 2021; Zhu et al., 2021). However providers should be reminded that the hemodynamic benefits of

remimazolam outweigh the small risk of lack of procedural success in fragile patients.

Although the utilization rates of remimazolam for endoscopic procedures in patients greater than 65 years old did not increase or decrease, chart review results did reveal a significant reduction ($P < 0.00045$) in the overall rates of hypotension following the educational intervention. This could be attributed to anesthesia providers increased knowledge of the benefits of remimazolam for elder patients with comorbidities, which therefore lead providers to reserve its use for fragile patients at higher risk for hemodynamic compromise. Due to the most agreed barrier that remimazolam is not as readily available as other anesthetics (often less is stocked in the pyxis than propofol), it may be necessary for anesthesia providers at this facility to spare its use for when most necessary. With providers utilizing remimazolam for sedation on the most appropriate patients, rates of hypotensive episodes were overall significantly decreased following the educational intervention.

Chart review data also revealed a significant difference in hypotensive rates when using propofol versus remimazolam for sedation. Patients receiving propofol had almost a 40% greater chance of experiencing hypotension than patients receiving remimazolam for sedation. This data corresponded with the research that propofol does have a higher incidence of hypotension (Sneyd et al., 2022). Data on other hemodynamic measures and neurologic recovery were not as significant. There was not enough data regarding respiratory depression or hypoxia rates to draw any conclusions on this information. Data on neurologic recovery was assessed through length of PACU stay. Overall, remimazolam prolonged PACU stay by 6 minutes on average. However, this data was not significant enough to suggest that remimazolam definitively trends toward prolonged PACU stay or prolonged neurologic recovery. Overall, even with the lack of significant data regarding secondary hemodynamic outcomes, the significance of data on rates of

hypotension can be used to encourage providers to choose an anesthetic that is safer for patients and improves patient outcomes.

Limitations

There are several limitations to this project. This project yielded a small sample size of anesthesia providers who participated, which is mostly due to the small rural hospital size. An educational intervention on a larger group of anesthesia providers from multiple facilities may provide more generalized data. Separation of providers may have also provided more insight on increase in use for individual providers versus generalizing practice change to the entire group of anesthesia providers. Another limitation of this study includes the narrow number of chart reviews. An increased amount of patient data to analyze would have generated more meaningful outcomes. Additionally, providers at this facility were very experienced in providing anesthesia. Therefore they have a more established routine and comfort of how they do things, which may require additional education to prompt change in their practice. A final limitation is the use of paper charting during the time of this project. Anesthesia providers recorded vital signs by hand every 5 minutes, and they were not transferred in real time or minute by minute. This creates opportunity for important hemodynamic data such as hypoxia, hypotension, or respiratory depression to be missed if it happens during the 5-minute paper documentation gap.

Future Recommendations

The use of remimazolam in the targeted patient population seemed to improve rates of hypotension and patient outcomes. To facilitate an increase in the use of remimazolam, there are several recommendations for future practice. Remimazolam should remain stocked in the pyxis' that providers use during endoscopic procedures. There should be enough remimazolam to use throughout the day since there are often several endoscopic procedures scheduled in one room

each day. Furthermore, anesthesia providers should be reminded that adverse effects of hemodynamic compromise while providing anesthesia on fragile patients can lead to increase costs. Although the cost of remimazolam is slightly greater, using it for high-risk patients may prevent adverse events and therefore decrease costs while increasing patient safety. Additionally, participation in regular evidence-based practice (EBP) education conferences and/or incorporating EBP education in staff meetings may be beneficial in keeping experienced anesthesia providers up to date on current practice recommendations that improve patient outcomes. Barriers to increasing the utilization of remimazolam were identified and presented to the anesthesia leaders at this facility. Future recommendations were also discussed with the chief anesthetist in effort to increase the application of EBP into practice by the anesthesia providers at this facility.

Conclusion

This DNP project aimed to increase provider knowledge on the benefits of using remimazolam for sedation in patients greater than 65 years old undergoing endoscopic procedures and change anesthesia provider practice in effort to improve patient outcomes. Present research encourages the use of remimazolam for endoscopic procedures in patients over the age of 65 to reduce hemodynamic compromise and improve outcomes for fragile patients. Following an educational intervention, anesthesia providers displayed an understanding that remimazolam does improve patient outcomes compared to propofol. Although the use of remimazolam did not increase or decrease, patient outcomes did improve. This could be due to increased provider knowledge and therefore a better selection of patients to receive remimazolam for sedation during endoscopic procedures. Continued education can improve utilization and patient outcomes and as more evidence becomes available, the benefits of using remimazolam for elderly patients undergoing endoscopic procedures will increase. This should lead to

increased utilization and improved patient outcomes in the future.

Appendix A

Recruitment Flyer

15 SEPTEMBER 2023

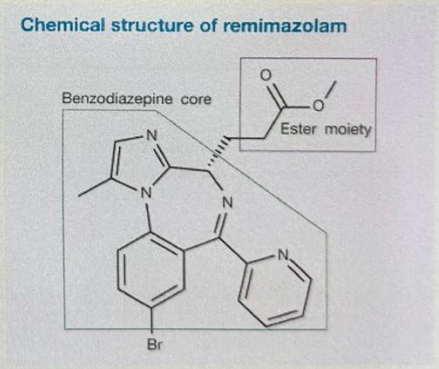
learn more about REMIMAZOLAM

the benefits of remimazolam use for endoscopic procedures

presentation by
Holly Nunn, UNCG SRNA

please join for a brief educational session

light breakfast and coffee will be provided



will take place in the consult room just past the surgical waiting room | 06:15am

Appendix B

Educational Handout

REMIMAZOLAM (BYFAVO)

Benefits of its use for colonoscopy, endoscopy, TEE, or bronchoscopy procedures.

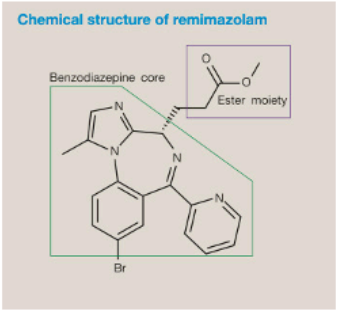
Problem:

Side effects of currently used anesthetics for endoscopic procedures.

- Propofol: hypotension, respiratory depression, pain on injection
- Fentanyl: respiratory depression
- Midazolam: prolonged neurologic recovery

Elderly patients or those with multiple comorbidities are at a higher risk of adverse events from the negative side effects of common anesthetics.

Pharmacokinetics/Pharmacodynamics:



Derived from midazolam: GABA-A agonist
Extra carboxylic ester linkage

- Metabolized by plasma and tissue esterase

Onset: 1-1.5 minutes
Peak sedation: 3-3.5 minutes after first bolus dose
Time to fully alert: 11-14 minutes

Dosing:

ASA I-II
Initial bolus dose: 5mg over 1 minute
Maintenance: 2.5mg over 15 seconds (every 2 minutes or longer as needed)

ASA III-IV
Initial bolus dose: 2.5-5mg over 1 minute
Maintenance: 1.25-2.5mg over 15 seconds (every 2 minutes or longer as needed)

Benefits:

Adequate sedation
No pain on injection
Minimal hypotension
Decreased incidence of hypoxia
Rapid neurologic recovery

Appendix C

Educational Intervention Script

Introduction:

Good morning! For those of you who don't know me, my name is Holly Nunn and I am a third year anesthesia student at UNC Greensboro. I went to Appalachian State for my BSN and started my nursing career here at Watauga in the critical care unit. I have had the opportunity to shadow and hangout in the OR with you guys' anesthesia team several times over the years, which is when I was introduced to remimazolam. When I started the doctoral program, I knew I was going to have to come up with an idea for my DNP project. I started to do some research on remimazolam and found the results to be very interesting. So, I chose to do my DNP project on the benefits of using remimazolam as the anesthetic choice for endoscopic procedures such as colonoscopy, endoscopy, TEE, and bronchoscopy, which is what I am here to share with you.

Current problem:

- During my practicing anesthesia as an SRNA I have observed that the patient population typically served, especially for endoscopic procedures, are patients above the age of 65. With that being said, we all know that comorbidities tend to increase in the aging population, aka these are some of the more fragile patients.
- While propofol has been and is a phenomenal drug, it does come with side effects that I am sure you guys are all familiar with - hypotension, decreased respiratory rate, airway obstruction, and even apnea. These side effects are even more prominent in the elderly population and those with significant comorbidities.
- Probably less commonly used but still worth mentioning the lingering mental effects of Versed, and respiratory depression potential of narcotics like fentanyl.
- These side effects often seem transient and benign but can also lead to detrimental adverse events.
- So, if there is a better alternative that produces the same adequacy of sedation yet decreases the amount of side effects, why not use it?

Pharmacokinetics/Pharmacodynamics:

(reference photo of remimazolam chemical structure on handouts)

Just a few housekeeping facts about how remimazolam works.

- It is derived from midazolam, so it works on the GABA-A receptor in the brain the same way. The difference is it has an extra carboxylic ester linkage (which you can see in the photo on your handout the remimazolam chemical structure)… all that to say that remimazolam is independent of organ metabolism and is metabolized by plasma esterase which allows for rapid recovery.
- I'm sure many of you may be a little more familiar with remifentanil, and this "soft drug" approach – which is the addition of the ester linkage - is also what was taken to develop remifentanil to allow its rapid on/offset. Just to give you a little more familiar example of how the drug works.
- The onset of sedative effects of remimazolam is around 1-1.5 minutes, and the average time to peak levels of sedation after the first bolus dose is around 3-3.5 minutes.
- Average time to fully alert after the last dose is around 11-14 minutes.

Dosing:

- For those of you who are already using and are familiar with remimazolam, dosing information may be repetitive and unnecessary. I just want to briefly run through the reconstitution and dosing recommendations for those who may not be as familiar with the drug so maybe you can feel more comfortable if you choose to use it in the future.
- Remimazolam comes in a 20mg vial as a powder form to be reconstituted. The recommendation from Acacia Pharma is to dilute the powder with 8.2ml NS, which will yield a 10ml syringe remimazolam with final concentration of 2.5mg/ml.
    - But can also dilute however you would like, diluting in 20ml syringe will yield 1mg/ml which is perfectly fine.
- Reconstitution can seem inconvenient when assigned to fast paced procedures like endo, TEEs or bronchs all day, but the good news is that if you are planning to use remimazolam for your patients, you are still able to pre-draw syringes. They are good to use for 8 hours after being reconstituted.
- Induction of anesthesia: recommended dose is 5mg bolus over 1 minute
    - For ASA III-IV: 2.5-5mg bolus
- Maintenance of anesthesia: recommended 2.5mg bolus over 15 seconds

    - For ASA III-IV: 1.25-2.5mg
- Re-dose for maintenance of anesthesia every 2 minutes, or longer as needed.
- Of course the same as our other anesthetics, this medication is also titrate to effect. So just adjust this dose dependent upon your assessment of the patient to determine exact dosages.

Statistics:

My research on remimazolam focused on its utilization for endoscopic procedures. So as I mentioned earlier this would include upper endoscopy, colonoscopy, bronchoscopy, or TEE.

- I know as anesthetists our purpose is to sedate each patient adequately enough for the surgeon to complete the procedure so it's important to all of us that whatever anesthetic we choose can provide proficient sedation.
    - Remimazolam can induce sedation as quickly as propofol when higher doses are given for the initial bolus.
    - Two large study results showed a 96.9% and 96.5% success rate (success rate meaning which did fall slightly short to propofol at 100%.
    - But if we are weighing benefits and risks it may still be appropriate to choose the safer anesthetic even with this low percentage risk of aborting the procedure.
- Patient satisfaction is also part of our responsibility, so any preventable discomfort should ideally be avoided.
    - 3 out of 5 patients experience pain with injection of propofol, 1 out of 5 say this pain is excruciating.
    - Multiple large studies noted that remimazolam does not produce burning at the injection site.
- Most importantly, hemodynamic stability has proven to be increased when utilizing remimazolam as the primary anesthetic.
    - Remimazolam has significantly lower rates of hypotension compared to propofol which is important for all patients, but especially the elderly and those with several comorbidities.

    - In endoscopic procedures where we do not have an airway in place it can be difficult to maintain the airway throughout the procedure especially when the patient has episodes of respiratory depression, apnea, or obstruction.
    - Incidence of hypoxia was considerably less in patients who received remimazolam versus propofol.
- Finally, neurologic recovery with remimazolam is obviously significantly faster than midazolam, and comparable to propofol. So use of this anesthetic should not prolong wake-up times, or PACU time.
- In that our primary goal is to provide adequate sedation as safely as possible for the patient, remimazolam seems to be a good fit for anesthetic choice in these patients.

Costs:

- Propofol ~ $9.20 per 200mg (20ml) vial
- Byfavo ~ $41.67 per 20mg vial
- Currently there is only brand name (Byfavo) available, but hopefully in the future there could be a cheaper generic option.

Sources:

Appendix D

Post-Intervention Survey

Please select your gender:	Male ☐ Female ☐				
Please indicate how long you have been a providing anesthesia as a certified registered nurse anesthetist:	< 1 year ☐ 1-5 years ☐ 5-15 years ☐ > 15 years ☐				
In the **LAST MONTH**, how often did you practice anesthesia for endoscopic procedures (endoscopy, colonoscopy, bronchoscopy, or TEE)?	Daily☐ 2-3x Weekly☐ 2-3x Monthly☐ Never☐				
	Never	**Rarely**	**Occasional**	**Frequently**	**Very Frequently**
I have incorporated the use of remimazolam more in my practice of taking care of patients undergoing colonoscopy, endoscopy, bronchoscopy, or TEE.					
When compared to propofol, remimazolam decreases incidence of (based on your experience):	**Strongly Disagree**	**Disagree**	**Neither Disagree**	**Agree**	**Strongly Agree**
Hypotension					
Respiratory depression					
Hypoxia (O2 saturation)					
Pain on Injection					
Prolonged Neurologic Recovery					

Please continue to the back of this survey →

Please select the answer most applicable to your practice	**Strongly Disagree**	**Disagree**	**Neither Disagree**	**Agree**	**Strongly Agree**
I believe remimazolam ***has adverse*** effects on patients undergoing endoscopic procedures.					
My colleagues ***do not*** support the use of remimazolam for endoscopic procedures.					
I need to see more evidence-based support in the literature to integrate the presented interventions into my practice.					
Remimazolam is not as readily available as other anesthetics.					
Having to reconstitute remimazolam ***decreases*** my use of the drug.					
I am ***not*** comfortable using a less familiar anesthetic when providing sedation for patients undergoing endoscopic procedures.					
Remimazolam costs more than other primary anesthetic choices.					
I will continue to utilize remimazolam for sedation in fragile patients undergoing endoscopic procedures.					
Please indicate any other barrier(s) that are not addressed that you have encountered when implementing the presented intervention for anesthetic management of patients undergoing endoscopic procedures					

References

Acacia Pharma Incorporated. *Rapid Onset/Offset Benzodiazepine with CYP450-Independent Metabolism*. Byfavo® (remimazolam). (2023). https://byfavo.azurewebsites.net/pharmacology

Ahuja, S., Mascha, E. J., Yang, D., Maheshwari, K., Cohen, B., Khanna, A. K., Ruetzler, K., Turan, A., & Sessler, D. I. (2020). Associations of Intraoperative Radial Arterial Systolic, Diastolic, Mean, and Pulse Pressures with Myocardial and Acute Kidney Injury after Noncardiac Surgery. *Anesthesiology*, *132*(2), 291–306. https://doi.org/10.1097/ALN.0000000000003048

Antonik, L. J., Goldwater, D. R., Kilpatrick, G. J., Tilbrook, G. S., & Borkett, K. M. (2012). 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. *Anesthesia and Analgesia*, *115*(2), 274–283. https://doi.org/10.1213/ANE.0b013e31823f0c28

Bickler, P. E., Feiner, J. R., Lipnick, M. S., Batchelder, P., MacLeod, D. B., & Severinghaus, J. W. (2017). Effects of Acute, Profound Hypoxia on Healthy Humans: Implications for Safety of Tests Evaluating Pulse Oximetry or Tissue Oximetry Performance. *Anesthesia & Analgesia*, *124*(1), 146–153. https://doi.org/10.1213/ANE.0000000000001421

Chen, S., Wang, J., Xu, X., Huang, Y., Xue, S., Wu, A., Jin, X., Wang, Q., Lyu, J., Wang, S., Li, Y., Yu, Y., Ai, D., Luo, A., Min, S., Li, L., Zou, X., Liu, J., Lv, P., … Zhang, J. (2020). The efficacy and safety of remimazolam tosylate versus propofol in patients undergoing colonoscopy: A multicentered, randomized, positive-controlled, phase III clinical trial. *American Journal of Translational Research*, *12*(8), 4594–4603.

Dai, G., Pei, L., Duan, F., Liao, M., Zhang, Y., Zhu, M., Zhao, Z., & Zhang, X. (2021). Safety and efficacy of remimazolam compared with propofol in induction of general anesthesia. *Minerva Anestesiologica*, *87*(10), 1073–1079. https://doi.org/10.23736/S0375-9393.21.15517-8

Guo, J., Qian, Y., Zhang, X., Han, S., Shi, Q., & Xu, J. (2022). Remimazolam tosilate compared with propofol for gastrointestinal endoscopy in elderly patients: A prospective, randomized and controlled study. *BMC Anesthesiology*, *22*(1), 180. https://doi.org/10.1186/s12871-022-01713-6

Heuss, L. T., & Inauen, W. (2004). The Dawning of a New Sedative: Propofol in Gastrointestinal Endoscopy. *Digestion*, *69*(1), 20–26. https://doi.org/10.1159/000076543

Jalota, L., Kalira, V., George, E., Shi, Y.-Y., Hornuss, C., Radke, O., Pace, N. L., & Apfel, C. C. (2011). Prevention of pain on injection of propofol: Systematic review and meta-analysis. *BMJ*, *342*, d1110. https://doi.org/10.1136/bmj.d1110

Jhuang, B.-J., Yeh, B.-H., Huang, Y.-T., & Lai, P.-C. (2021). Efficacy and Safety of Remimazolam for Procedural Sedation: A Meta-Analysis of Randomized Controlled Trials With Trial Sequential Analysis. *Frontiers in Medicine*, *8*, 641866. https://doi.org/10.3389/fmed.2021.641866

Kim, S.-H., & Fechner, J. (2022). KoreaMed Synapse. *Korean Journal of Anesthesiology*, *75*(4), 307–315. https://doi.org/10.4097/kja.22297

Lin, O. S. (2017). Sedation for routine gastrointestinal endoscopic procedures: A review on efficacy, safety, efficiency, cost and satisfaction. *Intestinal Research*, *15*(4), 456–466. https://doi.org/10.5217/ir.2017.15.4.456

Liu, L., Gauri, D. K., & Jindal, R. P. (2021). The Role of Patient Satisfaction in Hospitals'

Medicare Reimbursements. *Journal of Public Policy & Marketing*, *40*(4), 558–570. https://doi.org/10.1177/0743915620984723

Liu, X., Ding, B., Shi, F., Zhang, Y., Liu, L., Sha, Y., & Zhao, T. (2021). The Efficacy and Safety of Remimazolam Tosilate versus Etomidate-Propofol in Elderly Outpatients Undergoing Colonoscopy: A Prospective, Randomized, Single-Blind, Non-Inferiority Trial. *Drug Design, Development and Therapy*, *15*, 4675–4685. https://doi.org/10.2147/DDDT.S339535

Montandon, G., & Slutsky, A. S. (2019). Solving the Opioid Crisis: Respiratory Depression by Opioids as Critical End Point. *CHEST*, *156*(4), 653–658. https://doi.org/10.1016/j.chest.2019.05.015

Novak, R. (2022b, March 24). *Remimazolam: New Wonder Anesthetic Drug or Medical White Elephant?*. The Anesthesia Consultant . https://theanesthesiaconsultant.com/2022/03/24/remimazolam/

Pastis, N. J., Yarmus, L. B., Schippers, F., Ostroff, R., Chen, A., Akulian, J., Wahidi, M., Shojaee, S., Tanner, N. T., Callahan, S. P., Feldman, G., Lorch, D. G., Ndukwu, I., Pritchett, M. A., Silvestri, G. A., & PAION Investigators. (2019). Safety and Efficacy of Remimazolam Compared With Placebo and Midazolam for Moderate Sedation During Bronchoscopy. *Chest*, *155*(1), 137–146. https://doi.org/10.1016/j.chest.2018.09.015

Rex, D. K., Bhandari, R., Desta, T., DeMicco, M. P., Schaeffer, C., Etzkorn, K., Barish, C. F., Pruitt, R., Cash, B. D., Quirk, D., Tiongco, F., Sullivan, S., & Bernstein, D. (2018). A phase III study evaluating the efficacy and safety of remimazolam (CNS 7056) compared with placebo and midazolam in patients undergoing colonoscopy. *Gastrointestinal Endoscopy*, *88*(3), 427-437.e6. https://doi.org/10.1016/j.gie.2018.04.2351

Rex, D. K., Bhandari, R., Lorch, D. G., Meyers, M., Schippers, F., & Bernstein, D. (2021). Safety and efficacy of remimazolam in high risk colonoscopy: A randomized trial. *Digestive and Liver Disease: Official Journal of the Italian Society of Gastroenterology and the Italian Association for the Study of the Liver*, *53*(1), 94–101. https://doi.org/10.1016/j.dld.2020.10.039

Shirey, M. R. (2013). Lewin's Theory of Planned Change as a Strategic Resource. *JONA: The Journal of Nursing Administration*, *43*(2), 69. https://doi.org/10.1097/NNA.0b013e31827f20a9

Sneyd, J. R., Absalom, A. R., Barends, C. R. M., & Jones, J. B. (2022). Hypotension during propofol sedation for colonoscopy: A retrospective exploratory analysis and meta-analysis. *British Journal of Anaesthesia*, *128*(4), 610–622. https://doi.org/10.1016/j.bja.2021.10.044

Ul-Haque, I., Shaikh, T. G., Ahmed, S. H., Waseem, S., Qadir, N. A., Bin Arif, T., & Haque, S. U. (2022). Efficacy of Remimazolam for Procedural Sedation in American Society of Anesthesiologists (ASA) I to IV Patients Undergoing Colonoscopy: A Systematic Review and Meta-Analysis. *Cureus*, *14*(3), e22881. https://doi.org/10.7759/cureus.22881

Wesselink, E. M., Kappen, T. H., Torn, H. M., Slooter, A. J. C., & van Klei, W. A. (2018). Intraoperative hypotension and the risk of postoperative adverse outcomes: A systematic review. *British Journal of Anaesthesia*, *121*(4), 706–721. https://doi.org/10.1016/j.bja.2018.04.036

Zhang, J., Cairen, Z., Shi, L., Pang, S., Shao, Y., Wang, Y., & Lu, Z. (2022). Remimazolam versus propofol for procedural sedation and anesthesia: A systemic review and meta-analysis. *Minerva Anestesiologica*, *88*(12). https://doi.org/10.23736/S0375-

9393.22.16817-3

Zhu, X., Wang, H., Yuan, S., Li, Y., Jia, Y., Zhang, Z., Yan, F., & Wang, Z. (2021). Efficacy and Safety of Remimazolam in Endoscopic Sedation-A Systematic Review and Meta-Analysis. *Frontiers in Medicine*, *8*, 655042. https://doi.org/10.3389/fmed.2021.655042