Perioperative Risks

- Reduced responsiveness to vasopressor, potential risk of rebound Htn in withdrawal (potential risks in general/neurologic/vascular surgery).
- Potential risk of ARF in major bleeding and kidney ischemia.

Induction/Maintenance

- Watch for refractory hypotension, which requires treatment with a vasopressin agonist.

Adjuvants/Regional Anesthesia/Reversal

- No known interactions

Postoperative Period

- Resume preop drugs for BP control if no ARF
- Only available in "per os" forms

Anticipated Problems/Concerns

- Recommended preop withdrawal for 24–48 h

Antianxiety Medications

Ijeoma Nwachukwu | Lee A. Fleisher

Uses

- Preop anxiolysis, anterograde amnesia, IV sedation, IV induction of anesthesia, suppression of seizure activity, muscle relaxation

Perioperative Risks

- Sedation
- Respiratory depression
- Apnea
- Airway obstruction
- Delayed emergence
- Delirium

Worry About

- Potentiation of respiratory depression with opioids

Overview/Pharmacology

- Benzodiazepines (midazolam and diazepam) are the most commonly used antianxiety medications in the periop period.
- Benzodiazepines:
  - Highly lipid-soluble, allowing a rapid onset of action and quick termination of effects.
  - Antianxiety effect via activation of the GABA receptor by binding to the gamma subunit.
  - Metabolized in the liver by microsomal oxidation or glucuronide conjugation.
  - Effects can be reversed by flumazenil, a selective benzodiazepine antagonist.

Drug Class/Mechanism of Action/Usual Dose

- Benzodiazepines
- GABA activator
- Chronically taken for generalized anxiety, panic attacks, muscle spasms, phobias
- Acutely taken for periop anxiolysis, IV sedation, induction of general anesthesia, seizures
- Anxiolysis dose for midazolam is 1–2.5 mg IV q5 min or 0.07–0.08 mg/kg IM q30–60 min
- Alternatives: Other benzodiazepines (clonazepam, alprazolam), beta blockers (propranolol), tricyclic antidepressants (amitriptyline), SSRIs (duloxetine), anticonvulsants, propofol

Drug Effects

System	Effect	Assessment by Hx	PE	Test
CNS	CNS depression, decreased cerebral metabolic rate, decreased cerebral blood flow, decreased seizure activity	Headache, anterograde amnesia		
CV	Decreased SVR, decreased systolic BP		Hypotension	ECG
RESP	Dose-dependent respiratory depression, decreased ventilatory response to CO_2	Drowsiness, sedation	Hypoventilation, apnea, hiccoughs, cough	ABG
GI	Decreased to increased N/V		Increased secretions	
DERM	Eruptions	Pain at IV injection site, pruritus, burning	Erythema Hives	
Toxicity				
CV	Cardiac arrhythmias including premature ventricular contraction, bradycardia, and tachycardia		Hypotension	ECG
RESP	Respiratory arrest, airway obstruction, laryngospasm, bronchospasm		Apnea, shallow respirations	ABG
DERM	Thrombophlebitis	Pruritus	Hives	
CNS	Unconsciousness, physical dependence, anterograde amnesia		Unresponsiveness, delirium, dysphoria	

Key References: Olkkola KT, Ahonen J: Midazolam and other benzodiazepines, *Handb Exp Pharmacol* 182:335–360, 2008; Eilers H: Intravenous anesthetics. In Miller RD, Pardo M editors: *Basics of anesthesia*, 6th ed. Philadelphia, 2011, Elsevier, pp 99–114.

Perioperative Implications

Preoperative Concerns

- Antianxiety medications have a synergistic effect with opioids and propofol and may potentiate respiratory depression, leading to airway obstruction or respiratory arrest.
- Effects of benzodiazepines can be prolonged in the elderly and in pts with severe liver disease.

Induction/Maintenance

- Benzodiazepines can be used for the induction of general anesthesia. A dose of 0.1–0.3 mg/kg of midazolam is sufficient to produce unconsciousness.
- When administered with other induction agents, benzodiazepines decrease the speed of induction and decrease minimal anesthetic concentration MAC requirements.

Reversal

- Effects of benzodiazepines can be reversed by flumazenil, a benzodiazepine antagonist.

Anticipated Problems/Concerns

- Flumazenil has a shorter half-life than benzodiazepines; hence medication should be redosed to avoid resedation.