Alternative Medications for Procedural Sedation (Adults ≥18 Years of Age)

Introduction
The Society of Critical Care Medicine’s Drug Shortages Task Force has developed a guideline for procedural sedation that can be referred to for other options if a drug shortage arises with a particular class of medications. When utilizing less familiar medications for this indication, it is recommended to review basic principles of procedural sedation:

- Goals for sedation and analgesia:
  - Alteration of patient level of consciousness, mood and anxiety level
  - Amnesia of unpleasant sensation
  - Increase in pain threshold
  - Patient cooperation with appropriate response to tactile and verbal stimulation
  - Maintenance of intact airway
  - Maintenance of protective airway reflexes
  - Hemodynamic stability

- Procedural sedation is classified based on patient assessment into four categories:
  - Minimal sedation/analgesia: mild anxiolysis or pain control
  - Moderate sedation: purposeful response following voice or light touch
  - Deep sedation: purposeful response following painful stimuli
  - General anesthesia: no purposeful response to repeated painful stimuli

- Level of sedation can be an unpredictable, dynamic process based on pharmacokinetic and pharmacodynamic principles; therefore, it is recommended that providers utilizing unfamiliar medications be prepared to rescue patients from depth of sedation beyond the intended level based on institutional standards.

- Use of anesthetic induction agents, including methohexital, propofol, and ketamine, should be consistent with institutional standards for deep sedation, regardless of route of administration and intended level of sedation.

- Characteristics of an ideal drug for procedural sedation and analgesia:
  - Predictable pharmacokinetic profile
  - Rapid onset of action
  - Analgesic and anxiolytic effects
  - Short recovery time
  - Minimal associated risks
  - Consider the patient’s comorbidities when selecting drug, dose and administration interval, as patients with coexistent disease, extreme age, obesity, sleep apnea, and renal or hepatic insufficiency are more likely to develop complications associated with procedural sedation.

- May be administered without the presence of an anesthesiologist

- Providers should make a distinction between analgesics that relieve pain (Table 1) and sedatives that decrease anxiety and promote somnolence (Tables 2 and 3).

- If both benzodiazepines and analgesics are used, consider:
  - Dose reduction of both agents
  - Giving an opioid first and titrating benzodiazepine to desired depth of sedation to minimize the risk of respiratory depression

- Reversal agents, including naloxone and flumazenil, should be available whenever opiates or benzodiazepines are administered.

- Continued monitoring is recommended as the duration of action of the reversal agent(s) may be less than that of the agent it is intended to reverse.

Table1: Analgesia*
<table>
<thead>
<tr>
<th>Drug</th>
<th>Pharmacologic Class</th>
<th>Approximate Parenteral Equianalgesic Dose</th>
<th>Onset (IV) (min)</th>
<th>Duration</th>
<th>Initial Dosing: Intermittent</th>
<th>Initial Dosing: Continuous Infusion</th>
<th>Repeat Dosing/ Titration</th>
<th>Side effects</th>
<th>Reversal</th>
<th>Safety Implications</th>
<th>Special Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fentanyl</td>
<td>Opioid</td>
<td>0.1 mg (100 mcg)</td>
<td>1-2</td>
<td>30-60 min (duration prolonged with higher doses)</td>
<td>0.5-1 mcg/kg IV</td>
<td>NA</td>
<td>May repeat every 15-30 minutes (consider using lower ¼ to ½ of initial dose)</td>
<td>Bradycardia, potentiated with propofol</td>
<td>Naloxone</td>
<td>Respiratory depression may last longer than analgesia</td>
<td>Less hypotension compared to morphine</td>
</tr>
<tr>
<td>Hydromorphone</td>
<td>Opioid</td>
<td>1.5 mg</td>
<td>1-3</td>
<td>2-4 hrs</td>
<td>0.5-1.5 mg IV</td>
<td>NA</td>
<td>May repeat every 15-30 minutes</td>
<td>Nausea, vomiting, hypotension, bradycardia, pain at injection site, local tissue irritation</td>
<td>Naloxone</td>
<td>Potential for potency-related dosing errors</td>
<td>Accumulates with hepatic and renal impairment, which leads to an increased duration of effect</td>
</tr>
<tr>
<td>Morphine</td>
<td>Opioid</td>
<td>10 mg</td>
<td>5-10</td>
<td>2-4 hrs</td>
<td>0.05-0.1 mg/kg IV or 2-4 mg IV</td>
<td>NA</td>
<td>May repeat every 15-30 minutes (max 15 mg)</td>
<td>Hypotension, bradycardia bronchospasm, pruritus, vomiting, chest wall rigidity</td>
<td>Naloxone</td>
<td>Side effects can be due to histamine release</td>
<td>Accumulates with hepatic and renal impairment, which leads to increased duration of effect</td>
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<tr>
<td>Remifentanil</td>
<td>Opioid</td>
<td>0.1 mg</td>
<td>1-1.5</td>
<td>3-10 min</td>
<td>NA</td>
<td>Loading dose: 0.5 mcg/kg IV</td>
<td>Adjust by 0.025 mcg/kg/min every 5 min (max of 0.2 mcg/kg/min)</td>
<td>Apnea, respiratory depression, chest wall rigidity, hypotension, bradycardia, post procedure nausea and vomiting.</td>
<td>Discontinue therapy</td>
<td>Risk of apnea and hypoventilation; only practitioners trained with airway management and anesthetic agents should administer</td>
<td>Potency similar to fentanyl Ultra short acting Clearance unchanged with renal/hepatic insufficiency Not suitable as the sole agent for induction and should be used in conjunction with other agents In obese patients (&gt;130% of IBW), use IBW for dosing</td>
</tr>
</tbody>
</table>

*Rapid titration of opiates may lead to hypotension and/or respiratory depression; #Tiers represent the order in which alternative agents should be considered.*
<table>
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<tr>
<th>Drug</th>
<th>Pharmacologic Class</th>
<th>Onset (min)</th>
<th>Duration (min)</th>
<th>Initial Dosing: Intermittent</th>
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<tr>
<td><em>Tier 1</em></td>
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<tr>
<td>Midazolam (IV)</td>
<td>Benzodiazepine</td>
<td>1-3</td>
<td>30-80</td>
<td>0.02 mg/kg IV (2 mg IV increments)</td>
<td>NA</td>
<td>May repeat every 3-5 minutes (max 0.2 mg/kg IV total)</td>
<td>Hypotension, respiratory depression, paradoxical agitation</td>
<td>Flumazenil</td>
<td>Use with caution in patients who are obese or have acute kidney injury/chronic renal failure due to risk of accumulation of the active metabolite with repeated dosing; clearance is reduced when administered with medications that inhibit cytochrome P₄₅₀ enzyme systems. Reduce dose 25-50% if combined with opioids.</td>
<td>Consider patient-specific variables when determining dosage</td>
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<tr>
<td><em>Tier 2</em></td>
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<tr>
<td>Lorazepam (IV)</td>
<td>Benzodiazepine</td>
<td>15-20</td>
<td>360-480</td>
<td>0.02-0.05 mg/kg IV or 1-2 mg IV</td>
<td>NA</td>
<td>0.5-1 mg IV every 15-20 minutes (max 4 mg IV)</td>
<td>Hypotension, respiratory depression, paradoxical agitation</td>
<td>Flumazenil</td>
<td>Due to slower onset and longer duration of action, has limited utility in procedural sedation. Reduce dose by 25-50% if combined with opioids.</td>
<td>Consider patient-specific variables when determining dosage</td>
</tr>
<tr>
<td>Dexmedetomidine (IV)</td>
<td>α₂-receptor agonist</td>
<td>15 (following start of infusion)</td>
<td>60-120</td>
<td>NA (see safety implications)</td>
<td>0.6-0.7 mcg/kg/hr IV</td>
<td>Adjust by 0.1-0.2 mcg/kg/hr at least every 30 min (usual range 0.2-1.5 mcg/kg/hr)</td>
<td>Bradycardia, hypotension</td>
<td>NA</td>
<td>Use with caution in patients with a history of heart block and those dependent on adrenergic tone to maintain blood pressure. Bolus dose increases risk of bradycardia, hypotension, and/or hypertension</td>
<td>While dexmedetomidine provides mild analgesia, it will not blunt noxious stimuli and should not be used without adequate analgesia Can cause loss of oropharyngeal muscle tone; monitor for hypoxemia and hypoventilation (effects can be enhanced with concomitant benzodiazepine use)</td>
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<tr>
<td><em>Tier 3</em></td>
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<tr>
<td>Nitrous Oxide (Inhaled)</td>
<td>Anesthetic Gas</td>
<td>2-5</td>
<td>5</td>
<td>NA</td>
<td>25-50%</td>
<td>NA</td>
<td>Decreased myocardial contractility, worsening pulmonary hypertension, nausea, peripheral neuropathy, headache, CNS excitation, ↑ intracranial pressure</td>
<td>NA</td>
<td>Requires a well-ventilated room and has potential for provider exposure or abuse; gas scavenging system minimizes provider exposure Can increase pressure in closed gas containing spaces pockets of air (e.g., pneumothorax, pneumoperitoneum / bowel obstruction, intraocular pressure, inner ear pressure, endotracheal tube cuff pressure)</td>
<td>Administer with 30% oxygen to avoid diffusion hypoxia; oxygen should be continued after nitrous oxide discontinued. Typically used as adjunct to other sedatives.</td>
</tr>
</tbody>
</table>

*Tiers represent the order in which alternative agents should be considered; NA: not applicable*
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<th>Duration (min)</th>
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<tbody>
<tr>
<td>Propofol</td>
<td>Sedative hypnotic</td>
<td>1</td>
<td>5-10</td>
<td>0.5-1 mg/kg IV</td>
<td>NA</td>
<td>0.5-1 mg/kg IV every 5 min</td>
<td>Pain at injection site, hypotension, myocardial depression, bradycardia, apnea, hypersensitivity reaction (allergy to eggs or soy), hypertriglyceridemia</td>
<td>NA</td>
<td>Small or large dose changes may result in an unpredictable general anesthetic state. Initial hypotension exaggerated when administered via central access.</td>
<td>Providers should be prepared to rescue patients from depth of sedation beyond the intended level. Institutional procedures or state laws may preclude bolus administration by nurses.</td>
</tr>
<tr>
<td>Etomidate</td>
<td>Sedative hypnotic</td>
<td>1</td>
<td>5-15</td>
<td>0.1 mg/kg IV</td>
<td>NA</td>
<td>1-2 mg IV every 10 min</td>
<td>Emergence nausea/vomiting, adrenal suppression, myoclonous/seizure activity</td>
<td>NA</td>
<td>Use caution in patients at risk for adrenal insufficiency. Due to short duration of action, role in therapy may be for shorter procedures.</td>
<td></td>
</tr>
<tr>
<td>Ketamine</td>
<td>Dissociative anesthetic</td>
<td>0.5</td>
<td>5-10</td>
<td>1-2 mg/kg IV</td>
<td>NA</td>
<td>0.2-0.5 mg/kg IV every 10 min</td>
<td>Emergence delirium, increased systemic and pulmonary pressures, intracranial and intraocular pressures, laryngospasm, hypersalivation, tachycardia</td>
<td>NA</td>
<td>Use caution in patients with significant coronary artery disease, increased intracranial/intraocular pressure and excessive respiratory secretions. Consider pretreatment with anti-sialogogue to minimize secretions.</td>
<td>Consider pre-treatment with benzodiazepines to prevent associated emergence reactions. Institutional procedures or state laws may preclude bolus administration by nurses.</td>
</tr>
<tr>
<td>Methohexital</td>
<td>Barbiturate</td>
<td>1-3</td>
<td>5-10</td>
<td>0.75-1 mg/kg IV</td>
<td>NA</td>
<td>0.5 mg/kg IV every 2-5 min</td>
<td>Hypotension, myocardial depression, CNS and respiratory depression</td>
<td>NA</td>
<td>Unpredictable general anesthetic state may result, particularly with large doses.</td>
<td>Providers should be prepared to rescue patients from depth of sedation beyond the intended level.</td>
</tr>
</tbody>
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References:


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