Ketamine for ICU Analgesia and Sedation

Ketamine inhibits N-methyl-D-aspartate (NMDA) receptor activity, inhibits gamma aminobutyric acid (GABA), blocks opioid receptors, and alters neurotransmitter concentrations. These mechanisms afford ketamine potent analgesic, sedative, and bronchodilatory activity. Ketamine has been most commonly used for its dissociative amnestic properties during short emergency medicine procedures in children and adults. Ketamine is also used with other agents for rapid sequence intubation, anesthesia induction, refractory status asthmaticus, acute pain, chronic pain syndromes, in some Enhanced Recovery After Surgery (ERAS) protocols, to treat refractory agitation while managing acute stimulant intoxication, and in patients with status epilepticus.

Interest in ketamine for analgesia and sedation in critical care patients is also growing. The chart below reviews ketamine use in the ICU for analgesia and sedation, answering common questions about patient selection, dosing, administration, and monitoring.

**Abbreviations**: ICU = intensive care unit; IV = intravenous.

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| When can ketamine be used for ICU analgesia and sedation? | • Ketamine may be a safe and effective option in select ICU patients [Evidence Level B-1]. Think of ketamine as an adjunct to standard therapies or in place of standard therapies (e.g., when hypotension and bradycardia limit use of fentanyl, propofol, dexmedetomidine) for ICU analgesia and sedation.  
• Certain types of patients may respond more favorably to ketamine in light of the drug’s side effect profile, such as patients with:  
  o underlying chronic obstructive pulmonary disease (COPD), asthma, or in acute pulmonary disorders like pneumonia and acute respiratory distress syndrome (ARDS)  
  o low blood pressure or heart rate, and/or shock  
  o uncontrolled pain, opiate-related hyperalgesia, or dose-limiting opiate-related side effects  
• Although ketamine may cause slight elevations in intracranial pressure, it has been used safely in head trauma patients, possibly due to ketamine increasing cerebral perfusion. |
| Who should not receive ketamine? | • The side effect profile of ketamine can be problematic in patients with certain comorbidities. Contraindications to ketamine may vary among facilities or protocols. Examples of possible contraindications include:  
  o history of severe allergic reaction to ketamine  
  o hypertensive emergency  
  o decompensated heart failure  
  o cardiac ischemia  
  o pulmonary hypertension  
  o risk for psychotic behavior, including schizophrenia and alcohol withdrawal |
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| How is ketamine dosed for ICU analgesia and sedation?                  | • There are limited data available to provide specific ketamine dosing guidance. Follow your facility protocols.  
• Protocols for patients receiving ketamine in the ICU for analgesia and sedation often include:  
  o bolus doses given before starting continuous infusions (e.g., 0.5 to 1 mg/kg; 1 mg/kg often limited to patients on a ventilator).  
  o infusions of about 0.5 to 1 mg/kg/hour (doses may range from 0.1 to 4.5 mg/kg/hour).  
    ▪ When used in an opioid-sparing capacity, expect lower ketamine doses (e.g., 0.05 to 0.5 mg/kg/hour).  
    ▪ Doses may be adjusted periodically (no more frequently than every 15 minutes), usually by 0.25 to 0.5 mg/kg/hour. Can consider slower adjustments with lower doses (e.g., 0.05 to 0.5 mg/kg/hour). |
| What side effects are associated with ketamine when used for ICU analgesia and sedation? | • Side effects may be more common with higher doses, and can include:  
  o psychomimetic side effects (e.g., emergence reactions [can include: anxiety, delirium, dream-like state, nightmares, illusions, or visual hallucinations], confusion, delirium).  
    ▪ Emergence reactions may not be as common with lower doses or in the elderly (e.g., >65 years old), but caution is still warranted.  
    ▪ Provide an appropriate environment and minimize stimuli during recovery to try to minimize emergence reactions (e.g., dim lighting, limit noise, have a comforting person present).  
  o hypertension and tachycardia  
  o hypersalivation and increased bronchial secretions  
    ▪ Some ketamine protocols may include treatment options for patients who develop excessive secretions (e.g., glycopyrrolate, scopolamine patch).  
  o twitching (may be confused with seizure activity, but not associated with electroencephalogram [EEG] changes)  
  o increased pressures, including intracranial, intraocular, and pulmonary airway  
  o respiratory depression, especially after large IV bolus doses |
| How should ketamine be administered and monitored for ICU analgesia and sedation? | • Facilities may have more than one protocol for ketamine due to different dosing strategies (e.g., ICU analgesia and sedation, procedural sedation, acute pain management), recommended monitoring, and who is approved to administer (e.g., nurses, prescribers).  
• Double check protocols to know who can administer, ketamine dosing, route of administration, and to be sure appropriate monitoring is followed.  
• **Administration**  
  o Usually give bolus doses as short infusions or IV push over at least 60 seconds. Quicker administration may be associated with more respiratory depression.  
  o Ketamine continuous infusions can be mixed in 250 or 500 mL of normal saline or 5% dextrose injection. The standard final concentration is 1 mg/mL to 2 mg/mL. Infusion rates will vary based on dose and concentration being used. |

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| ICU administration and monitoring, continued | - **Monitoring** may vary among facilities, hospital locations, and with doses used. Follow facility protocols for monitoring. Expect monitoring for patients receiving ketamine in the ICU by continuous infusion to include:⁴⁻⁵,¹⁸  
  - hemodynamic and cardio-pulmonary monitoring (e.g., blood pressure, heart rate, telemetry, oxygen saturation)  
  - assessments for the emergence of signs of increased agitation or delirium  
  - pain scale and sedation monitoring (to assist with dose titration and/or tapering)  
  - increased secretions monitoring  
  - Watch for ketamine accumulation and oversedation, especially with infusions used >24 hours or in obese patients.⁵  
  - Ketamine crosses the blood brain barrier and may accumulate in morbidly obese patients due to its lipophilicity.⁵ |
| What drug-drug interactions are important with ketamine? | - Watch for additive sedation and prolonged recovery upon discontinuation when combined with other sedative meds (e.g., benzodiazepines, barbiturates, opioids).³  
  - Look for cytochrome P450 (CYP) drug interactions with ketamine, as it is metabolized in the liver by CYP3A4, CYP2B6, and CYP2C9.³⁵ See our chart, *Cytochrome P450 Drug Interactions*, for details on meds that inhibit (may enhance effects) or induce (may reduce effects) of these specific enzymes. |
Levels of Evidence

In accordance with our goal of providing Evidence-Based information, we are citing the LEVEL OF EVIDENCE for the clinical recommendations we publish.

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| A     | Good-quality patient-oriented evidence.* | 1. High-quality RCT  
2. SR/Meta-analysis of RCTs with consistent findings  
3. All-or-none study |
| B     | Inconsistent or limited-quality patient-oriented evidence.* | 1. Lower-quality RCT  
2. SR/Meta-analysis with low-quality clinical trials or of studies with inconsistent findings  
3. Cohort study  
4. Case control study |
| C     | Consensus; usual practice; expert opinion; disease-oriented evidence (e.g., physiologic or surrogate endpoints); case series for studies of diagnosis, treatment, prevention, or screening |

*Outcomes that matter to patients (e.g., morbidity, mortality, symptom improvement, quality of life).

RCT = randomized controlled trial; SR = systematic review


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References

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