Michigan Medicine

Ketamine IV Continuous Infusion Guidelines for Mechanically Ventilated Adult ICU Patients

Background

Ketamine is a N-methyl-D-aspartate receptor (NMDA) antagonist that creates a state of dissociative amnesia in patients. It is used frequently used for as an anesthetic for procedural sedation and in the operating room, as well as an induction agent rapid sequence intubation. Recent literature has suggested that ketamine may be an effective sedative agent in mechanically ventilated patients. It has also been studied in patients suffering from alcohol withdrawal, status asthmaticus, and status epilepticus.

Pharmacokinetics

Absorption: 100% IV absorption

Distribution: 5-16 L/kg (increased in critically ill patients)

Onset: Less than one minute

Metabolism/Excretion: CYP3A4 and CYP2D6 mediated metabolism via N-demethylation and hydroxylation to norketamine and dehydronorketamine. Norketamine is an active metabolite with ~33% potency of ketamine; dehydronorketamine is an inactive metabolite.

Half-Life: Ketamine = 5-17 minutes, norketamine = 180-300 minutes

Pharmacodynamics

Ketamine primarily acts as an antagonist to the NMDA receptor, although it also has some antagonistic effects of delta, kappa, and mu receptors as well. Ketamine also inhibits re-uptake of catecholamines, which can yield an increase in blood pressure.

Considerations

ICU attending approval required for continuous infusion ketamine use

Ketamine should be used cautiously in patients with:

- Uncontrolled hypertension
- Pulmonary hypertension
- Moderate-severe hepatic dysfunction (Child-Pugh Class B and C)
- History of coronary artery disease
- Atrial arrhythmias
- Concomitant use of strong CYP3A4 and CYP2D6 inhibiting medications
- Patients with pre-existing history of schizophrenia or bipolar disorder
Contraindications

- Allergy to ketamine
- Active coronary ischemia

Adverse Effects

- Hypertension
- Hyper salivation
- Transient respiratory depression
- Agitation
- Ketamine emergence reactions

Management: Hyper salivation may be managed via the administration of glycopyrrolate 0.4 mg IV Q6H as needed. Emergence reactions may be managed with the administration of a benzodiazepine, either lorazepam 1-2 mg IV or midazolam 2-4 mg IV as needed. Hypertension is best managed by decreasing rate or stopping ketamine infusion; no studies to date have described management of ketamine-induced hypertension with antihypertensive agents.

Indications and Dosing

Sedation in adults who cannot tolerate other agents: Continuous infusion of 0.2 – 1.2 mg/kg/hr. Recommended initial rate is 0.2 mg/kg/hr. Titrate by 0.1 mg/kg/hr every 15 minutes to goal RASS.

Status Asthmaticus: Optional bolus dose of 0.5 mg/kg (max 50 mg) followed by continuous infusion of 0.5 – 2.5 mg/kg/hr. Recommended initial rate is 0.5 mg/kg/hr. Titrate by 0.1 mg/kg/hr every 15 minutes to clinical response.

Alcohol Withdrawal: Optional bolus dose of 0.3 mg/kg (max 30 mg) followed by continuous infusion of 0.15-0.30 mg/kg/hr. Recommended initial rate is 0.15 mg/kg/hr. Titrate by 0.05 mg/kg/hr every 15 minutes to clinical response.

Status Epilepticus: Optional 1.5 mg/kg loading dose (150 mg max) followed by 1-10 mg/kg/hr continuous infusion. Starting rate and titration are at the discretion of ICU team only.


Ketamine dose may titrated down to off quickly over the period of 60 minutes if necessary due to adverse events or for an awakening trial

Dose Adjustments

*Renal Dysfunction: Due to the primarily hepatic metabolism of ketamine, dose does not need to be adjusted for renal dysfunction. Ketamine has been administered to patients with ESRD without effects of dose accumulation noted.

**Hepatic Dysfunction: To date, no studies have been conducted demonstrating that ketamine can be used safely in patients with moderate-severe hepatic dysfunction. However, given that ketamine is
predominantly hepatically metabolized, use in this population certainly puts patients at risk for accumulation of ketamine and the drug should be used with caution in these patients.

**Monitoring Parameters**

Check blood pressure, respiratory rate, sedation level, and pain score prior to and once 15-30 minutes following bolus dose, initiation of infusion, or infusion dose change. While on continuous infusion, check blood pressure, respiratory rate, sedation level, pain score, and SpO₂ once every 4 hours.

Ketamine cause vivid dreams, hallucinations, and anxiety. These adverse effects may be managed with as needed benzodiazepines. However, discontinuation or avoidance of ketamine may also be necessary in patients experiencing these adverse effects. Ketamine may contribute to development of ICU delirium, although incidence is not well-described. Ketamine should be used cautiously in patients with a pre-existing history of psychiatric illness.

**Administration**

Continuous infusion intravenous ketamine may be administered through either a peripheral or central line.

**Orderable**

Ketamine 10 mg/mL 50 mL infusion bag

**References:**


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