Low Dose Ketamine for Pain Control



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Purpose of Education

- Introduce the pharmacology of ketamine when used as an adjunct therapy agent in pain control.
- Identify patients who may benefit clinically from low dose ketamine administration for pain control purposes.
- Instruct the clinician on the contraindications, side effects, dosing parameters, administration guidelines, and patient monitoring.

Historical Background and Evidence Based Research

- Ketamine is a dissociative medication which distorts perceptions of sight and sound and produces feelings of detachment. It has been widely used for anesthesia/sedation purposes.
- In the 1980s, ketamine's pain control properties were discovered.
- Research has shown the use of ketamine to be effective in treating a variety of conditions including: depression, status epilepticus, status asthmaticus, severe agitation, opioid tolerant pain, and chronic narcotic use.
- In response to the documented research, there has been an increased interest across healthcare specialties in the use of low dose ketamine as an adjunct therapy for patient pain control.

Historical Background and Evidence Based Research

• Ketamine has been shown to be safe and effective in treating a wide variety of pain conditions.

This includes pain exacerbations in opioid tolerant patients.

- There is less potential for addiction or overuse.
- Ketamine has less effect on a patient's respiratory system compared to opioids, thereby decreasing complications associated with respiratory depression.

Use of Low Dose Ketamine

Pain Control/Analgesia:

- Treatment of fractures, abdominal pain, back pain, trauma, burns, cholecystitis, malignancy, sickle cell anemia/crisis, neuropathic pain, and postoperative pain
- Intraoperatively as an adjunct therapy
- Adjunct analgesic agent in ED and critical care areas
- Short term therapy only (48 hours)
- Approved locations for low dose ketamine: ED, ICU, PACU and Day Hospital Pediatrics

Ketamine Analgesia: Patient Selection

Moderate to severe pain:

- Refractory pain previously treated with opioids (failed opioid trial)
- Patient in a methadone treatment program
- Opioid tolerant patient or chronic opioid user
- Opioid induced hyperalgesia
- Opioid allergy
- Sickle cell crisis pain
- Patient at risk for hypoventilation
- Hemodynamically unstable patient (e.g. trauma patient)
- Elderly

Analgesia Mechanism of Action

- N-methyl-D-aspartate (NMDA) receptor antagonist
 - Both analgesic and anesthetic effects
- Ketamine has a direct effect on opioid receptors
 - It augments activity of opioid mu-receptor function, which *lowers* opioid doses for the same effect
 - Ketamine is *not* reversed by naloxone (Narcan)
- Ketamine affects α-1 and β-2 receptor agonists
 - This allows for hemodynamic stability
 - For some, use of ketamine may lead to hypertension

Pharmacokinetics

• Half life:

- Distribution half life 10-15min
- Elimination half life approximately 2 hours

• Onset and Duration:

- \circ Onset 1 to 1.5 minutes
- Duration up to 60 minutes for analgesic effects

• Metabolized through the liver

Effects of Ketamine

Cardiac:

- Increases blood pressure, heart rate, and cardiac output, especially after bolus infusion
- Increases pulmonary artery pressure and myocardial workload
- Use cautiously in patients with Coronary Artery Disease, Hypertension, CHF, and Aneurysms

Respiratory:

 Apnea and respiratory depression associated with rapid administration IV bolus or high dose

NOTE: Rapid IV bolus or high dose ketamine is only administered by a credentialed physician or advanced practice provider

Effects of Ketamine

Neurologic:

- *Increases* cerebral oxygen consumption
- Increases cerebral blood flow
- Does *not* increase intracranial pressure
- Induces analgesia/pain control

Psychotropic Symptoms:

- 30% of patients treated with low dose ketamine may experience emergence reactions as it wears off
 - Disturbing dreams, delirium, anxiety, agitation, hallucinations, dysphoria, and psychosis
 - Symptoms resolve quickly
 - Patients with psychiatric history (PTSD) are at a higher risk
 - Pretreatment with benzodiazepines is *not* required

Contraindications and Precautions

Contraindications:

- Allergy to ketamine
- Significant hypertension
- Poorly controlled or severe cardiovascular disease
- Pregnancy
- Active psychosis
- Severe hepatic dysfunction

Precautions:

- Pulmonary Hypertension
- CHF
- Ischemic heart disease
- Tachycardia
- Schizophrenia
- Increased intra-ocular/intracranial pressure
- Traumatic brain injury
- Intracranial bleed
- Stroke
- Alcohol intoxication

Prescribing and Administering Low Dose Ketamine

Prescribing:

 Those trained in the induction and maintenance of sedatives with credentials and training in airway management

Administrating Nurse:

- RN with current ACLS or PALS certification
- Can monitor the patient receiving low doses for pain and titrate the infusion rate based on direction from credentialed provider

Practice for the administration of *low dose* ketamine for analgesia is approved by the State Board of Nursing

Ketamine Concentrations

- Product Concentration: 500mg/10ml (50mg/mL)
- Loading dose: 0.3mg/kg in 100mL NS (50mL NS in Pediatrics)
- **Continuous Infusion Concentration**: 1mg/1mL
 - Pharmacy will round dosages per BayCare Protocol
 - Pharmacy will compound all doses and hand deliver to the approved units (Emergency Department, Critical care, PACU, Day Hospital Pediatrics)
- Intranasal: drawn up undiluted into a syringe
 - Intranasal and IV push are administered by credentialed physician or advanced practice provider only

Low Dose Ketamine for P	ain Control: Adult Dosing

Route	Loading or Initial Dose	Repeat Dose or Continuous infusion	Maximum Dose
IV intermittent medication	 0.3mg/kg[*] in 100mL Normal Saline Administer over 15 minutes 	Repeat X 1 in 2 hours if needed (refer to pain scale)	0.5mg/kg
Continuous Infusion	 0.3mg/kg* in 100mL Normal Saline Administer over 15 minutes * May use lower starting dose of 0.1-0.2mg/kg 	 500mg/500mL (24hr bag) Concentration: 1mg/mL Start at 0.1mg/kg/hr Titrate by 0.05mg/kg/hr every 15 min to achieve pain relief (refer to pain scale); hold for RASS less than -1 Treatment Duration: 48hrs 	0.5mg/kg/hr
Intranasal	 1mg/kg undiluted Concentration: 50mg/mL Maximum dose: 100mg (1ml or 50mg per nostril) via mucosal automation device (MAD) By credentialed physician or advanced practice provider ONLY 	May repeat after 15 minutes	2 doses or 200mg

Low Dose Ketamine for Pain Control: Pediatric Dosing

Route	Loading or Initial Dose	Repeat Dose or Continuous infusion	Maximum Dose
IV intermittent medication	 0.3mg/kg[*] in 50mL Normal Saline Administer over 15 minutes 	Repeat X 1 in 2 hours if needed (refer to pain scale)	0.5mg/kg
Continuous Infusion	 0.3mg/kg* in 50mL Normal Saline Administer over 15 minutes * May use lower starting dose of 0.1-0.2mg/kg 	 100mg/100mL Normal Saline Concentration: 1mg/mL Start at 0.1mg/kg/hr Titrate by 0.05mg/kg/hr every 15 min to achieve pain relief (refer to pain scale); hold for RASS less than -1 Treatment Duration: 48hrs 	0.5mg/kg/hr
Intranasal	 1mg/kg undiluted Concentration: 50mg/ml Maximum dose: 100mg (1ml or 50mg per nostril) via mucosal automation device (MAD) By credentialed physician or advanced practice provider ONLY 	May repeat after 15 minutes	2 doses or 200mg

Nursing Administration

- Low dose ketamine is administered intravenously via an infusion pump
 - o Intermittent dose is infused over 15 minutes
 - **Continuous** infusion rate is not to exceed 0.5mg/kg/hr
- Doses used for pain control **fall below** the anesthesia and sedation doses
 - Per Florida Board of Nursing, ketamine can be administered by nursing in the intensive care setting - "up to 50mcg/kg/min, but generally 25mcg/kg/min or less for pain control or sedation"
- Ketamine IV push or intranasal is administered by a credentialed physician or advanced practice provider only

Patient Monitoring

• Vital Signs:

- HR, BP, RR, oxygen saturation, pain score and sedation score Q1 hour x 4, then Q4 hours and PRN
- Medication Hold Parameters:
 - Hold for RASS less than -1 and RR less than 14 breaths/minute
- Continuous Telemetry Monitoring:
 - Patients will be in the ED, ICU, PACU, or Day Hospital Pediatric setting
- Assess for Mental Status Changes:
 - Excessive sedation, psychotic/psychotropic symptoms, tonic-clonic movements
- Discharge or transfer:
 - Hold until hemodynamically stable and able to manage own airway
- Caution:
 - Ketamine has an additive or compounding effect with use of CNS or respiratory depressants

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