



Ketamine for Analgesia in Non-Intubated Patients in the Neuro-ICU

Who is the protocol appropriate for?

1. Patients who are awake, non-intubated, following commands and protecting their airway.
2. Must be able to use verbal numerical rating scale for pain.
3. Patients who have acute pain for which opioids would like to be avoided.

Contraindications: Ketamine should not be used if patient:

- is tachycardic (>120) or is hypertensive (>180 systolic)
- develops chest pain and/or elevated troponin, EKG changes
- has significant oral secretions

The Protocol: all patients monitored with every 1 hour neuro checks. RASS should be -1 to 0, airway adjuncts at bedside including nasal trumpet, supplemental oxygen.

1. **Ketamine infusion:** Start with a bolus of 0.25 mg/kg then start infusion at 2 mcg/kg/min. May titrate every 15 minutes by 1 mcg/kg/min to max of 15 mcg/kg/min for pain above patient tolerable threshold on pain scale. Maximum infusion period is 48 hours.

Down-titrating of ketamine: decrease infusion by 1 mcg/kg/min hourly for pain score below tolerable level for 2 consecutive hours.

Pain score assessed hourly and with drip titration based on verbal numerical rating scale. Tolerable level is number 0-10 that is acceptable level of discomfort for the patient

2. **Benzodiazepines:** to help prevent psychomimetic effects of ketamine. Give first dose in conjunction with starting ketamine: lorazepam: 1-2mg IV every 8 hours (dose dependent if < or >50kg)
3. **Opioid adjunct:** do not start until patient is at 10 mcg/kg/min ketamine
 - First choice: hydromorphone**
 - 0.3 mg IV q1 hour for pain over tolerable level but < 6 on VNRS
 - 0.6 mg IV q1 hour for pain 6-10 on VNRS
 - Second choice: fentanyl**
 - 25 mcg IV q1 hour for pain > tolerable but < 6 on VNRS
 - 50 mcg IV q1 hour for pain 6-10 on VNRS

Contact MD on call if pain still not controlled with these methods.

Monitoring Parameters:

Notify MD if:

- HR <50 or >120
- SBP <90 or >180
- RR <8 or >25
- Patient not able to be easily aroused/not following commands (RASS < -1)
- Significant increase in oral secretions
- Concern for significant psychomimetic effects (ie., hallucinations) causing mental distress to the patient

Rationale: Patients in the neuro-ICU can have pain for a variety of reasons including post-operative and related to traumatic injuries. Often times large doses of opioids are needed and pain is still not adequately controlled. There are now several adjuncts being used to help control pain in patients with the goal being to limit opioid use and help stop the pain cycle. Ketamine is a non-competitive NMDA antagonist which blocks neuronal Ca²⁺ influx preventing excitatory release and hyperexcitability. When NMDA receptors are activated, this causes a positive feedback loop which can lead to hyperalgesia, allodynia and increase pain radiation. Ketamine can also bind to opioid receptor but the function there is not known and it is not reversed by naloxone.

There are a number of randomized placebo controlled studies that have looked at ketamine dosing both pre-op and post-op compared to placebo which show longer time to first narcotic dose post-op as well as overall lower narcotic requirements. Ketamine is also used in palliative pain control in oncology patients as well as patients with chronic pain syndromes. Ketamine IV has very rapid onset (seconds) and half-life of 2-3 hours. It does have an active metabolite of norketamine which is more pronounced when ketamine is dosed orally. Only 4% is excreted unchanged in urine.

There are some side effects to ketamine, mostly sympathomimetic effects causing increased heart rate and blood pressure and nausea/vomiting. There are also some psychomimetic effects (hallucinations/delusions/nightmares). These are reported mostly at anesthetic doses (>1 mg/kg) but have been seen at lower doses as well. Benzodiazepines are often dosed with ketamine to prevent the psychomimetic effects.

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