

A Prospective Randomized, Double-Dummy Trial Comparing IV Push Low Dose Ketamine to Short Infusion of Low Dose Ketamine for Treatment of Pain in the ED

Background:

- Ketamine is an effective alternative to opiates for the indication of acute pain management
- Administration of ketamine via IV push, however, is associated with significant side effects such as feelings of unreality, sedation, nausea, vomiting and dizziness, which makes it unattractive to patients

Objective:

- To compare the adverse effects, sedation level and analgesic efficacy of low-dose ketamine between IV push administration and short infusion administration for acute pain in the ED

Methods:

- **Design:** Prospective, randomized, double-blind, double-dummy trial
- One-dose of ketamine with side effects measured for 120 minutes in most patients
- **Inclusion criteria:** patients had to be awake, alert and oriented to person, place and time; they had to be able to verbalize severity of pain and nature of adverse effects and they had to be able to understand the consent process and give consent
- **Exclusion criteria:** pregnancy, breast feeding, altered mental status, allergy to ketamine, weight <46kg or >115kg, unstable vital signs defined as: SBP <90 mmHg and >180 mmHg, pulse <50 bpm or >150 bpm and respirations <10 breaths/min or >30 breaths/min, PMH of acute head injury or eye injury, seizure, intracranial hypertension, renal or hepatic insufficiency, alcohol or drug abuse, psychiatric illness or recent (within 4 hours prior) analgesic use
- 24 patients were enrolled in the study
- **Primary outcome measures:** Overall rates as well as the specific severity levels of the side effects were measured, which were recorded in accordance with the Side Effects Rating Scale for Dissociative Anesthetics (SERSDA); severity of agitation and/or sedation was measured in accordance with the nine point Richmond Agitation-Sedation Scale (RASS)
- **Secondary outcome measures:** pain (based on the 11 point NRS scale), changes in vital signs and need for rescue analgesia
- The power of the study was 80%
- The data handling method was intention to treat

Results:

- 42 patients completed the study; 21 patients from each group
- **Primary outcome measures:** 91.7% of patients receiving IV push ketamine and 54.2% of patients receiving short infusion ketamine reported feelings of unreality, $P < 0.008$; IV push group showed a significantly greater degree of sedation at 5 min ($P = 0.01$)

- **Secondary outcome measures:** There were no differences in analgesic efficacy found between the two treatment methods during the study $P=0.14$; 8 patients in the IV push group and 7 patients in the short infusion group needed rescue morphine and this difference was not found to be significant; there were no significant changes in vital signs
- **Author's conclusion:** The authors concluded that IV low-dose ketamine given as a short infusion decreases rates of feeling of unreality and sedation in the first 15 minutes of administration without sacrificing analgesic effects

Strengths:

- Significant results
- Double-dummy design helped with blinding
- Adverse effects were statistically analyzed

Limitations:

- Single center study
- Small sample size
- Patients enrolled only between the hours of 8am-8pm Monday-Friday

Conclusion:

- Although this study showed that short infusion low dose ketamine resulted in less adverse effects than IV push low dose ketamine, ketamine is not actually used that often for the sole purpose of treating pain in the emergency room setting.
 - Opiates are used more frequently and are known to have less adverse effects.
- Short infusion ketamine is a good alternative for patients who cannot receive opioid therapy because of opiate addiction, intolerance or allergies.
- Future research: having a study with a larger sample size that compares ketamine with opioid analgesics to compare side effect rate and efficacy would be beneficial to determine ketamine's role in acute pain management going forward.

Reference: Motov S, Mai M, Pushkar I, Likourezos A, Drapkin J, Yasavolian M, et al (2017). A prospective randomized, double-dummy trial comparing IV push low dose ketamine to short infusion low dose ketamine for treatment of pain in the ED. AJEM. 2017; 35: 1095-1100.