

**Rory Stuart**

## **Block 6 CAT**

**Reference:** Beaudoin et al., Low-dose Ketamine Improves Pain Relief in Patients Receiving Intravenous Opioids for Acute Pain in the Emergency Department: Results of a Randomized, Double-blind, Clinical Trial. *Acad Emerg Med.* 2014 Nov;21(11):1193-1202

**Question:** Can low-dose Ketamine improve pain relief in patients who are receiving intravenous opioids for acute pain in the Emergency Department?

**Introduction:** Acute pain management in the Emergency Department is a constant challenge. Emergency providers must balance the need to relieve pain against the adverse effects of overmedication. In today's emergency department patient population the effects of significant levels of opioid tolerance makes this task even more daunting. Intravenous opioids are the mainstay of acute pain management in the ED; however, their use is often limited due to concerns for over sedation and more specifically respiratory depression. Ketamine, acts on a pain pathway unique from the opioids and therefore does not dampen respiratory drive, making it an attractive adjunct to acute pain management. Ketamine is already in use as a safe and effective component of perioperative pain management regimens.

**Methods:** This was a double-blind, placebo-controlled, randomized clinical trial that took place at the Rhode Island Hospital ED. This facility is a large urban level I trauma center with over 100K ED visits annually. Patient eligibility for the study was conducted by research assistants in the ED; inclusion criteria was a pain score greater than 5/10 and pain duration less than 7 days. After treating physician and patient consent was obtained patients were randomized into one of three groups; a morphine monotherapy group and one of two morphine/ketamine combination therapy groups (differing ketamine doses: 0.15 mg/kg vs 0.3 mg/kg). In the combination therapy groups patients first received IV morphine 0.1 mg/kg up to a dose of 10 mg, prior to the administration of ketamine.

**Results:** A total of 60 patients were ultimately included in the study (20 in each group). The primary outcome, pain relief, was measured using patient-reported pain scores. Pain scores were taken at 30 minutes, 1 hour, and 2 hours after initial administration of medications. While pain scores dropped across all group, the combination therapy cohorts had greater overall improvements in pain on the 2 hr course. There was no significant difference in scores between the two combined therapy groups. No behavioral disturbances, dysrhythmias or respiratory depression necessitating naloxone were reported in any group.

**Discussion:** This study, while small, did demonstrate that low-dose ketamine can be safely used as an effective adjunct to morphine in the ED management of acute pain. In any assessment of pain, both academic and clinical, there will always be limitations in the subjective nature of this data. The small numbers of enrolled patients also raises the question of power and may limit the applicability of this data to larger groups. A proposed molecular mechanism for the effectiveness of the combination therapy was briefly discussed. It has been proposed that morphine may activate NDMA receptors and trigger an antinociceptive effect. Ketamine, a NDMA receptor antagonist would, in theory, blunt this effect – very interesting but unfortunately a full discussion of these pathways were beyond the scope of this article.

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