Is low-dose ketamine an effective and safe alternative to opioids for treatment of acute pain in the emergency department?

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Ratings: Methods – 4/5 Usefulness – 3/5

INTRODUCTION

Background

Opioids have an established efficacy and safety profile for treating acute pain in the emergency department (ED). Low-dose ketamine may be a preferred analgesic option in opioid dependent or tolerant patient populations, or patients at high risk of opioid related respiratory depression. To consider alternative treatments, such as ketamine, similar efficacy and safety to opioids should be established.

Objectives

(1) Compare the short-term efficacy of ketamine administered as a single-agent intravenous (IV) bolus versus opioid analgesia for the treatment of acute pain in the ED. (2) Quantify risk of adverse events from using ketamine as opioid alternative.

METHODS

Design

Systematic review of randomized controlled trials (RCTs) comparing IV opioids with IV ketamine for pain control.

Eligibility criteria

RCTs published in English. No placebo comparison groups. No coadministration of another pharmacologically active substance less than 20 minutes after IV ketamine/opioid treatment.

Subjects

Adults (>18) presenting to ED with acute pain beginning within the past 7 days.

Intervention

IV ketamine (<0.5 mg/kg) for acute pain compared with IV opioids.

Outcomes

(1) Change in either visual analog scale or numeric rating scale (NRS) from baseline to a second pain score, at time point reported closest to 10 minutes after receiving medication. (2) Rates of reported adverse effects.

RESULTS

Three studies were found to meet eligibility criteria. Ketamine (0.3 or 0.5mg/kg) was found to be noninferior

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to morphine (0.1mg/kg) in reducing NRS pain scores (relative reduction = 0.42, 95% confidence interval, -0.70 to 1.54). The authors conclude that no severe adverse events occurred in any study; however, increased rates of nonsevere adverse events in ketamine groups were observed. Adverse events, such as disorientation, dizziness, dysphoria, were more common in the ketamine treatment groups.

APPRAISAL

Strengths

- Clear, focused, and relevant question
- Adherence to PRISMA reporting guidelines and checklist
- Sensible eligibility criteria
- Comprehensive literature search
- Primary studies were generally low risk of bias
- No other psychoactive medications were coprescribed that may have affected analgesia efficacy or adverse effects experienced

Limitations

- Small number of patients (261 overall)
- Small number of primary studies (only three studies met inclusion criteria)
- Various adverse event categories reported by study precluded meta-analysis
- Variable timing for second pain scores documented by each study
- One study only included patients with acute pain from long-bone fractures
- The age range of patients (18–59 years) does not include pediatric/elderly populations

CONTEXT

The American College of Emergency Physicians include the use of ketamine in their policy on treating acute pain in the ED, stating that it may be used alone, or as part of multimodal therapy, to treat traumatic and nontraumatic pain.[1] Consensus guidelines from American Anesthesia and Pain Medicine groups suggest ketamine may be beneficial in patients with acute pain who are opioid tolerant, dependent, or at high risk for opioid-related respiratory depression (e.g., obstructive sleep apnea).[2] Giving ketamine by short infusion (15–20 minutes) by hanging a bag, or by infusion pump, may be more practical than remaining at bedside to give a push dose over 3–5 minutes and is associated with fewer neuropsychiatric side effects.[3]

BOTTOM LINE

This high-quality systematic review, with low rates of bias but only a total sample size of 261 patients, found low-dose ketamine (0.3 or 0.5 mg/kg) to be clinically noninferior to morphine (0.1 mg/kg) for treating acute pain in the ED. Ketamine was associated with higher rates of nonsevere adverse events, particularly neuropsychiatric symptoms, such as disorientation, dysphoria, and emergence reaction. Based on this study, and its support in clinical guidelines and policy, low-dose ketamine may be considered as an alternative to opioids for treatment of acute pain in the ED. Given its association with increased nonsevere adverse events, use of ketamine should be limited to when it may offer potential benefit over opioids, such as in patients with known opioid tolerance, dependence, or high risk of opioid related respiratory depression.

Keywords: Acute pain, analgesia, ketamine

Competing interests: None declared.

REFERENCES

1. American College of Emergency Physicians. "Optimizing the Treatment of Acute Pain in the Emergency Department." Policy Statement. Approved April 2017. From ACEP Policy on Optimizing the Treatment of Acute Pain in the Emergency Department, April 2017. Available at: https://www.acep.org/patient-care/policy-statements/optimizing-the-treatment-of-acute-pain-in-the-emergency-department. (accessed December 9, 2019).
2. Schwenk ES, Viscusi ER, Buvanendran A, et al. Consensus guidelines on the use of intravenous ketamine infusions for acute pain management from the American Society of Regional Anesthesia and Pain Medicine, the American Academy of Pain Medicine, and the American Society of Anesthesiologists. *Reg Anesth Pain Med*. 2018;43(5):456–66.
3. Motov S, Mai M, Pushkar I, et al. 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. *Am J Emerg Med*. 2017;35(8):1095–100.

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