TAKE-HOME MESSAGE

According to limited evidence, low-dose ketamine and morphine appear to provide similar levels of pain relief at 30 minutes; however, low-dose ketamine is associated with a higher rate of self-limited neuropsychological adverse events.

Is Low-Dose Ketamine an Effective Alternative to Opioids for the Treatment of Acute Pain in the Emergency Department?

EBEM Commentators
Michael Gottlieb, MD
Kelly W. Ryan, MD
Christine Binkley, MD, MPH
Department of Emergency Medicine
Rush University Medical Center
Chicago, IL

Results

The search identified 1,396 articles, of which 44 were deemed eligible for full-text review. Of these, a total of 8 articles (n=609 patients) were included in the final qualitative analysis. The review included 6 randomized controlled trials and 2 observational studies. Five studies were conducted in the United States, with the remainder conducted in France, India, and Iran. Most of the randomized controlled trials used low-dose ketamine, with doses ranging from 0.1 to 0.5 mg/kg given intravenously; however, one study followed the initial intravenous dose with a subcutaneous infusion at 0.1 mg/kg per hour. Another study that used a dose of 0.5 mg/kg gave patients concomitant midazolam at 0.3 mg/kg in the treatment group only. The comparator group included intravenous morphine at 0.05 to 0.1 mg/kg in all 6 of the included randomized controlled trials. In terms of analgesic effect, the 6 randomized controlled trials were rated as moderate quality, whereas the 2 observational studies were rated as very low quality.

Overall, moderate-quality studies did not demonstrate a significant difference in pain scores between the low-dose ketamine and opioids. There was insufficient evidence to determine whether low-dose ketamine reduced the need for rescue analgesia because of limitations of the data from the 3 studies assessing this outcome. There was an increased risk of adverse effects in the low-dose ketamine group compared with the morphine group (15.4% versus 4.4%). Adverse effects included agitation, hallucinations, dysphoria, and confusion; however, they were self-limited and there were no significant differences in rates of respiratory depression.

Commentary

Ketamine is a well-known agent used for procedural sedation in the ED, most commonly used in pediatric patients. Compared with other agents, ketamine offers the
Advantage of providing analgesia while protecting the respiratory drive. More recently, investigators have explored the use of subdissociative doses of ketamine (ie, low-dose ketamine) for acute pain management. Low-dose ketamine is typically considered to be doses of less than 1 mg/kg, although most studies use 0.1 to 0.3 mg/kg. Although there have been a number of studies performed in the postoperative setting that demonstrate evidence of a morphine-sparing effect, the evidence in the ED setting is limited.

This systematic review provides a qualitative analysis of 8 studies assessing the use of ketamine to treat acute pain in the ED setting. Although the results suggest that ketamine has efficacy similar to that of morphine, with a low rate of self-limited neuropsychiatric adverse effects, it is important to consider several limitations. First, the number of studies (N=4) and patients (n=225) assessing the ability of ketamine to reduce opioid use was small. Moreover, there were variations in the patient populations with respect to baseline characteristics and type of pain. There were also differences in the routes and doses of ketamine, as well as the use of adjuvant benzodiazepines and opioids. Furthermore, the outcome criteria varied significantly between trials, with differences in primary outcomes and methods of pain scale assessment (eg, numeric rating scale, visual analog scale, summed pain intensity difference). Finally, the definitions of adverse events were different between trials, with some providing empiric benzodiazepines to reduce the risk of emergence reactions.

Although this review provides preliminary evidence that low-dose ketamine may be used as an alternative to opioids for acute pain in the ED setting, studies with larger sample sizes and more rigorous methodology are needed to establish patient selection criteria and the best dosing strategy.

Editor’s Note: This is a clinical synopsis, a regular feature of the Annals’ Systematic Review Snapshot (SRS) series. The source for this systematic review snapshot is: Ghate G, Clark E, Vaillancourt C. Systematic review of the use of low-dose ketamine for analgesia in the emergency department. CJEM. 2017; https://doi.org/10.1017/cem.2017.48.


Michael Brown, MD, MSc, Jestin N. Carlson, MD, MS, and Alan Jones, MD, serve as editors of the SRS series.