DEM Journal Club

Article Appraisal

Article: Intravenous Subdissociative-Dose Ketamine Versus Morphine for Analgesia in the Emergency Department: A Randomized Controlled Trial

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Background and Study Objective(s):

Pain is one of the most common presenting complaints in the Emergency Department (ED). While opioid analgesics are commonly used, we are currently in the midst an opioid crisis where misuse and abuse of opioids has led to epidemic levels of addiction, overdose, and deaths. For this reason, many EDemergency clinicians are seeking other opioid-sparing options for pain control. Ketamine is an NMDA and glutamate receptor antagonist that is used in the ED for procedural sedation at higher doses, but at dissociative doses (0.1-0.6mg/kg), it maintains potent analgesic and amnestic effects with the preservation of airway reflexes, spontaneous respiration, and cardiopulmonary stability. Research from both the prehospital and in and outside of the ED settings hasve suggested that subdissociative doses of Kketamine can reduce pain while having an opioid sparing effect. This study aimed to determine if Kketamine at a dose of 0.3mg/kg would provide relief similar to morphine at 0.1mg/kg for acute moderate-severe pain in the ED setting.

Study Design:

This prospective, randomized, double-blind trial was completed in a community teaching hospital in New York City with an annual EDemergency census of 120,000 patients. A convenience sample of 90 patients was enrolled at multiple times per day. The pharmacist prepared 0.3mg/kg of ketamine or 0.1mg/kg of morphine in a 10mL syringe of NS according to a predetermined randomization list. The medication was delivered to the treating nurse in a blinded fashion who then administered the medication by IV push over 3-5 mins. Study investigators recorded pain scores, vital signs, and adverse effects at 15, 30, 60, 90, and 120 minutes. The primary outcome was comparative reduction of numeric rating scale (NRS) pain scores between recipients of ketamine and morphine at 30 mins. The secondary outcome was need for rescue analgesia at either 30 or 60 minutes. Vital sign changes and adverse events were also analyzed. An intention-to-treat analysis was employed.

Results:

All patients had significant reductions in mean pain at 15 and 30 minutes compared to baseline. In terms of the primary outcome of reduction in pain score at 30 minutes, there was no significant difference between groups

(mean difference 0.2, 95% CI -1.19 to 1.46). Patients in the Kketamine group did have higher rates of complete resolution of pain at 15 mins (percentage difference = 31%, CI 13%-49%). There was no difference between the 2 groups in rescue fentanyl at 30 minutes (percentage difference = 7%, 95% CI –3%-16%) or 60 minutes (percentage difference = –5%, 95% CI –18%-9%), but there was a difference of 17% for rescue fentanyl at 120 mins. While there were no serious adverse events in either group, more patients in the ketamine group reported dizziness and disorientation at the time of injection and at 15 mins compared to morphine recipients.

Validity of Results:

The results of this study were generally considered valid. This study did a number of things well. In particular, all clinically important outcomes were considered, participants were analyzed in the groups to which they were randomized, double-blinding was employed, and the treatment arm groups were similar. An important One consideration is that this study was powered based on two previous validation studies of pain rating scales with a sample size of 90,. and t There was modest degree of loss to follow up of reduction in enrolled patients leading to an overall number of 83 patients at 120 minutes. Fortunately, this attrition did not affect the primary outcome, but 2 patients were lost at 60 minutes. It is possible that a larger study would reveal a significant difference between groups.

Generalizability of Results:

As a single center study that used convenience sampling, the generalizability of this study is limited. The mean age was approximately 35 which may limit generalizability of these results to other ED patient populations. Specifically, is likely younger than the average emergency patient seen in our centers, and older patients (age >55) were excluded. Furthermore, there were several exclusion criteria that omitted patients who could benefit from subdissociative ketamine including those with chronic pain, drug abusers, and those with renal and hepatic toxicity.

The Bottom Line:

In ED patients with acute moderate to severe pain, use of analgesic dosing ketamine achieved a similar reduction in pain vs. morphine, but caused an increased number of side effects post injection and at 15 minutes that resolved by 30 minutes. Future studies may benefit from including It would have been useful to have included elderly patients, patients with substance use disorders, as well as patients with substance abuse disorder and those with chronic pain as these populations may benefit have much to gain from an opioid sparing approach to analgesia. Additionally, it would have been beneficial to know a little more about the patient experience in terms of symptom severity to make a meaningful assessment of the harm-benefit relationship. These are areas for further research.

Journal club attendees agreed that current utilization of sub dissociative Kketamine for pain in our centers varies, and many still prefer opioids as a first line treatment. Many recent studies support the effectiveness of low dose Kketamine in the ED as well as other health care settings. Overall, despite the low-risk profile of sub dissociative dose Kketamine, this study is not practice changing unless there are policies supporting its use in our EDs emergency departments. At many centers, sub dissociative dose Ketamine is grouped into the category of ‘sedation’ regardless of the dose, and therefore requires significant nursing time and frequent monitoring. This serves as a potential barrier to its regular operational use.

Overall it was felt that this study in isolation does not carry enough weight to encourage a shift to subdissociative ketamine first analgesia in these patients, especially given these feasibility issues in the ED, but it provides more support for the integration of subdissociative ketamine as another reasonable tool to consider in moderate to severe pain in the ED.