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Social Media

Hot Off the Press: Subdissociative-dose Ketamine for Acute Pain in the Emergency Department

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BACKGROUND

Safely and efficiently reducing pain are primary functions of emergency department (ED) providers.[1] Traditional analgesics (e.g., acetaminophen, nonsteroidal anti-inflammatory drugs [NSAIDs], opioids) often provide adequate relief, but managing refractory pain is challenging. Concerns for overtreatment and opioid abuse are balanced with the risk of oligoanalgesia.[2,3] Alternative nonopioid approaches to acute pain management are needed. Ketamine is an *N*-methyl-D-aspartate (NMDA) receptor antagonist typically used as a dissociative anesthetic.[4] However, subdissociative doses of ketamine (SDDK) effectively relieve acute perioperative[5] and chronic pain.[6] Ketamine's effectiveness in treating acute pain in the ED is worth exploring.

ARTICLE SUMMARY

This systematic review of randomized controlled trials (RCTs) evaluated SDDK compared with opiate or placebo for acute pain control in pediatric and adult patients.[7] Eligible trials used at least one dose of SDDK (defined as less than 1 mg/kg) and were identified through MEDLINE and EMBASE searches. Abstracts, reviews, unpublished reports, and non-English studies were excluded. The primary outcome was the change in pain score from patient arrival to the predetermined reassessment time. Secondary outcomes were the occurrence of adverse events, such as dissociative phenomena or nausea and vomiting and the reduction in consumption of opiates in patients who received SDDK. Four studies met eligibility criteria: three adult trials and one pediatric trial. In total, all four studies enrolled 428 patients. Three of the studies used ketamine 0.2 to 0.3 mg/kg/dose, while one used an infusion of 0.1 mg/kg/hour. Each study used a different comparison group. Using the Grading of Recommendations Assessment Development and Evaluation (GRADE) criteria, two reviewers evaluated study quality, of which three were deemed low quality and one moderate quality. Potential sources of bias included small sample sizes, lack of (or compromised) blinding, and lack of true randomization.

QUALITY ASSESSMENT

Only two electronic databases were used to identify potential studies. Exclusion of non-English RCTs, abstracts, and observational studies further threaten the complete identification of relevant literature. Inclusion of observational studies would have been particularly beneficial given the paucity of high-quality RCTs identified.

The quality of this systematic review is jeopardized by the failure to adhere to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) reporting guidelines (http://www.equator-network.org/). Furthermore, the GRADE instrument used was designed to weigh strength of evidence-based recommendations for guidelines. The Cochrane Risk of Bias tool was designed for systematic reviews of RCTs and may have been more appropriate.[8]

More concrete recommendations for future investigators regarding key questions and methodologic pitfalls would have been valuable to further define the role of SDDK for acute pain in the ED. Future investigations should use consistent ketamine[9] and comparator dosing, use a single pain scale to assess efficacy, stratify outcomes by pain etiology,[10] and adhere to Consolidated Standards of Reporting Trials (CONSORT) guidelines for monitoring and reporting of adverse events across studies.

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KEY RESULTS

Two of four trials reported significant reductions in pain. Another study reported "significantly lower pain scores," but did not provide absolute pain scores.[11] The sole pediatric study used the Observational Scale of Behavior Distress (OSBD) and reported scores of 1.08 (SD ± 1.12) versus 2.70 (SD ± 2.16) in ketamine and fentanyl groups, respectively ($p < 0.05$).[12]

The pediatric study reported increased incidence of vomiting when using ketamine with a number needed to harm of 17 (95% CI = 10 to infinity), meaning that for every 17 patients treated with ketamine versus fentanyl there will be one additional episode of vomiting, with precision for that estimate ranging from 10 to infinity. No increased vomiting was noted in adults. Another study reported significantly increased use of a rescue therapy when using morphine (18 of 20) as opposed to ketamine (0 of 20). Only one case of emergence phenomenon was observed across all four studies: a pediatric patient who recovered without intervention or hospitalization. Other cases of neuropsychological phenomena were reported, but the original articles lacked further description to determine if this referred to dissociation or emergence phenomena. Two studies demonstrated a significant reduction in opiate use by patients who received SDDK, although the clinical relevance of the reduced opiate use is unclear.

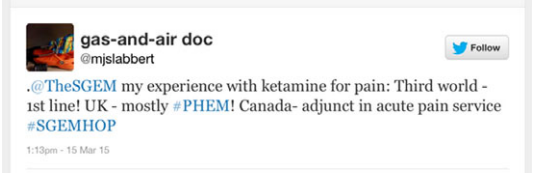
AUTHOR COMMENTS

The review article[7] was intended to foster interest in the topic of SDDK for acute pain based on existing published RCTs. The GRADE instrument was thought to be more easily understood by a diverse reader base than the PRISMA guidelines. The search strategy was limited to English-only RCTs because the authors wanted to limit the scope of the review to North American clinical practice. The authors used EMBASE and MEDLINE databases as their primary search engines, rather than the Cochrane Collaboration, because of their comfort with these databases. Papers from ClinicalTrials.gov were not considered given the authors' focus on completed research. Although the authors recognize the importance of observational studies and expert opinion, they were excluded due to the general consensus among the team that RCTs would provide the highest quality of evidence. Several areas for further research on the topic were identified, including evaluation of varying doses and routes of administration of SDDK and examination of how these variables may influence effectiveness and adverse events. Additionally, while the studies included in the systematic review evaluated SDDK's efficacy for musculoskeletal pain, a stratified analysis of SDDK's performance with other types of pain, such as neuropathic or visceral pain, may also be helpful for future clinical use.

TAKE-TO-WORK POINTS

Several additional SDDK RCTs[13,14] were published since this article, demonstrating the limited half-life of systematic reviews[15] given the rapid and continuous influx of new evidence. However, the authors were fair in their conclusions based on the literature available at the time of their search: current evidence for the use of SDDK for the control of acute pain is sparse, and what exists can neither authoritatively support nor refute its use. There seems to be a relatively low rate of SDDK-associated adverse events. High-quality RCTs are still needed to evaluate the effectiveness and safety of SDDK for acute pain in the ED. Although the use of SDDK in the ED for acute pain cannot be recommended routinely, consideration on a case-by-case basis is reasonable.

TOP 5 SOCIAL MEDIA COMMENTS



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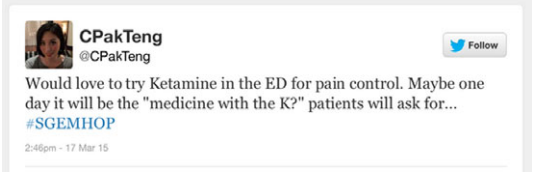

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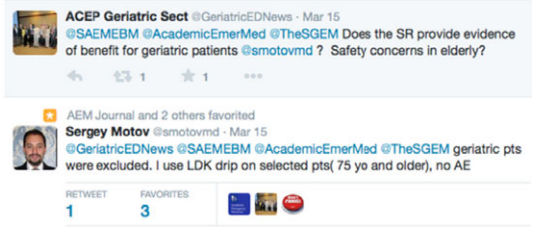

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"What a review! I use ketamine in ED and prehospital for analgesia. It's not perfect but it has advantages over opioids and NSAIDs." Minh Le Cong

https://www.facebook.com/TheSGEM?ref=ts&fref=ts

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