Ketamine as an Opioid-Sparing Strategy for Sickle Cell Vaso-Occlusive Crises in Pediatric and Adult Populations

Department of Anesthesiology & Critical Care Medicine, Interventional Pain Medicine, George Washington University School of Medicine and Health Sciences

Sarah A. Bokaee BA , Sina Davari MD

INTRODUCTION

Acute vaso-occlusive crises (VOC) are the leading cause of hospitalization in patients with sickle cell disease (SCD). While opioids remain the standard treatment, their adverse effects, tolerance, and potential for opioid-induced hyperalgesia have increased interest in opioid-sparing strategies that maintain effective pain control. Ketamine has emerged as a promising adjunct, but evidence remains limited and heterogeneous across pediatric and adult populations. We performed a systematic review evaluating its efficacy and safety for acute VOC.

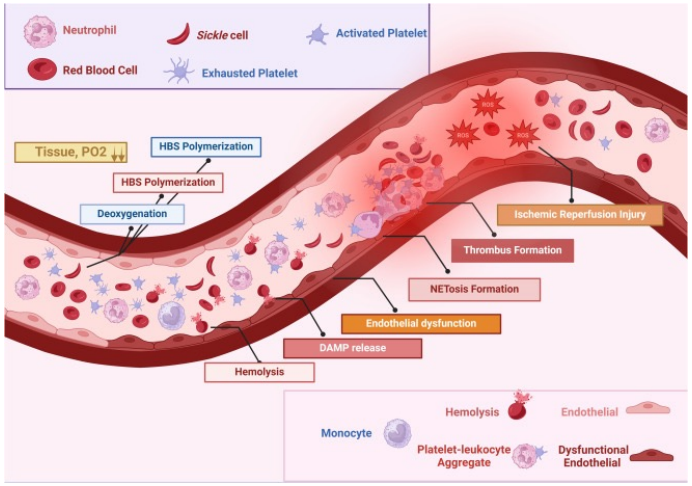


Figure 1. Mechanism of pain in vaso-occlusive crises in sickle cell patients.

MATERIALS & METHODS

A systematic review was conducted following PRISMA guidelines. PubMed and Google Scholar were searched using the term "ketamine sickle cell pain", yielding 54 records. After duplicate removal and screening, 14 studies met predefined inclusion criteria, including randomized controlled trials, prospective studies, retrospective cohorts, and case series evaluating ketamine for acute vaso-occlusive pain in pediatric or adult patients with SCD. Studies focused solely on implementation, utilization trends, or non-clinical outcomes were excluded. Data extracted included study characteristics, patient population, ketamine regimen, pain outcomes, opioid consumption, length of stay, readmission, and adverse events. Pediatric and adult studies were analyzed separately to account for differences in dosing strategies and clinical practice. Because this study synthesized previously published data and did not involve identifiable patient information, institutional review board approval and informed consent were not required.

RESULTS

Fourteen studies published between 2010 and 2026 met inclusion criteria, encompassing 4,682 patients. Seven studies evaluated pediatric or adolescent populations, six evaluated adults, and one evaluated both populations. Study designs included 2 randomized controlled trials, 4 comparative observational studies, 1 prospective study, and 7 retrospective case series/cohort studies. Sample sizes ranged from 5 to 3,391 patients. All studies evaluated intravenous ketamine, administered as either a single bolus (0.2–1 mg/kg) or continuous subanesthetic infusion (0.06 mg/kg/h to 5 µg/kg/min), most commonly as an adjunct to opioid therapy.

Across pediatric studies, 6 of 7 reported significant reductions in opioid consumption, while 5 of 7 demonstrated improved pain control. Among adult studies, 5 of 6 reported opioid-sparing effects and 4 of 6 demonstrated improved pain outcomes. Both randomized trials found ketamine provided analgesia comparable to morphine while reducing opioid requirements or cumulative morphine exposure. Studies evaluating earlier ketamine initiation consistently demonstrated improved clinical outcomes compared with delayed or rescue administration. Hospital length of stay was generally unchanged when reported. Adverse events were predominantly mild and transient, with hallucinations reported in 5.1%–23.9% of treated patients and treatment discontinuation reported in 0%–8.7% of cases. No study identified serious ketamine-related safety concerns or unexpected adverse events.

CONCLUSION

Intravenous subanesthetic ketamine appears to be a safe and effective opioid-sparing adjunct for acute vaso-occlusive pain in pediatric and adult patients with SCD. Current evidence demonstrates consistent reductions in opioid requirements with maintained or improved pain control. However, variability in dosing, timing, and treatment protocols limits definitive recommendations, and prospective multicenter studies are needed to establish standardized approaches and identify patient populations most likely to benefit.

REFERENCES

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