Safety and Utility of Continuous Ketamine Infusion for Sedation in Mechanically Ventilated Pediatric Patients

Amy L. Heiberger, PharmD; Surachat Ngorsuraches, PhD; Gokhan Olgun, MD; Lisa Luze, RN; Caitlin Leimbach, RN; Holly Madison, RN; and Saquib A. Lakhani, MD

OBJECTIVES The selection of sedative medications for mechanically ventilated pediatric patients remains an ongoing clinical challenge. Although continuous ketamine infusion has been used in this population, support for its use remains largely anecdotal. This study describes a single institution's use of ketamine infusions as part of a sedation protocol in the pediatric intensive care unit (PICU).

METHODS This was a retrospective study of children who received ketamine infusions as part of a multidrug sedation protocol in a 12-bed PICU at a tertiary children's hospital. Outcomes included effectiveness of ketamine infusion in providing adequate sedation as determined by State Behavioral Scale (SBS) scores and incidence of adverse events.

RESULTS A total of 22 children receiving ketamine continuous infusion as part of a multidrug sedation protocol from February 2014 through October 2015 were eligible and enrolled in the study. Ketamine continuous infusion was administered in addition to at least 2 other sedation infusions at an average rate of 1.02 ± 0.50 mg/kg/hr, with a range of 0.07 to 2.0 mg/kg/hr. The duration of ketamine was 65.7 ± 41.01 hours, with a range of 19 to 153 hours. There was no significant change in SBS scores before and after initiation of ketamine infusion. Although not statistically significant, patients with inadequate sedation prior to starting ketamine required fewer bolus sedation doses and had improved sedation after ketamine was started. There were no reported adverse events.

CONCLUSIONS The addition of a ketamine infusion as part of a multidrug sedation regimen was at least as effective as patients' regimen prior to ketamine addition in this population of intubated pediatric patients, with no adverse events.

ABBREVIATIONS NMDA, N-methyl-D-aspartate; PICU, pediatric intensive care unit; PRN, as-needed; PSP, PICU sedation protocol; SBS, State Behavioral Scale

KEYWORDS infusion; ketamine; mechanical ventilation; pediatric; sedation

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Introduction

The appropriate sedation of mechanically ventilated children in the pediatric intensive care unit (PICU) is central to ensuring patient comfort and safety. Opioids and benzodiazepines are frequently used as the primary medications for this indication and, while effective for many patients, they are associated with numerous adverse effects including hemodynamic instability, decreased gastrointestinal motility, delirium, and iatrogenic withdrawal. In addition, tolerance develops rapidly in many children and dose escalation or additional medications are needed to maintain an effective level of sedation. Therefore, while opioids and benzodiazepines remain the mainstay of sedative agents in the PICU, there continues to be a need for alternatives. Propofol infusion, which is common in adult ICU sedative regimens, is potentially problematic in children owing to the risk of severe metabolic

acidosis and cardiovascular collapse from propofol infusion syndrome.¹ More recently, dexmedetomidine use has increased for PICU sedation. Although this alpha-2 agonist has the distinct advantage of minimal respiratory depression, its side effect profile includes hypotension and bradycardia, which may limit its use in certain critically ill patients.²

Ketamine is a fast-acting general anesthetic with both analgesic and sedative activities that offers an additional option for sedation in mechanically ventilated PICU patients. Although ketamine is primarily known for its ability to block glutamate by antagonizing N-methyl-D-aspartate (NMDA) receptors, the exact mechanism of its action appears to be more complex, likely affecting a variety of cellular signaling pathways.^{3–6} It induces a dissociative state, provides effective anesthesia, and has rapid antidepressant effects. It has also been shown to maintain pulmonary compliance while reducing airway resistance,^{4,5} which has demonstrated

benefits in children with asthma. Unlike other sedation medications, ketamine has mostly beneficial effects on the cardiovascular system. It increases catecholamine concentrations through a combination of release and reuptake blockade, resulting in modest increases in heart rate, blood pressure, and cardiac output.^{4–6} However, in catecholamine-depleted states it may lead to hypotension when given as bolus dosing for induction. Ketamine may also cause emergence phenomena, often manifesting as vivid dreams and hallucinations.

Owing to its favorable profile on hemodynamic and respiratory functions, ketamine has been used for sedation of mechanically ventilated patients, though the evidence for its use in children remains scarce.^{5–8} In this study, we report the use of continuous ketamine infusion as a component of a standardized sedation protocol for mechanically ventilated children in the PICU.

Materials and Methods

Study Design and Patient Selection. This retrospective study describes intubated children who received ketamine via continuous infusion in a 12-bed multidisciplinary academic PICU in a 148-bed tertiary-care pediatric hospital. The PICU averages 775 yearly admissions and cares for a variety of medical and surgical cases. Although there is no cardiothoracic surgical service, children with underlying congenital heart disease are admitted for reasons other than cardiothoracic surgery. The study was approved by the local Institutional Review Board.

All patients admitted to the PICU from February 1, 2014, to October 31, 2015, who received continuous infusion of intravenous ketamine for at least 12 hours as part of the PICU Sedation Protocol (PSP) for mechanical ventilation were included. The PSP is a nurse-driven protocol in which physicians use a standardized electronic order set to designate continuous sedation infusions and as-needed (PRN) boluses. The goal endpoint is a targeted range determined by the prescriber on a well-studied and validated standardized sedation score, the State Behavioral Scale (SBS).⁹ The SBS uses a scale of –3 to +2 to define the level of sedation from –3 (unresponsive), –2 (responsive to noxious stimuli), –1 (responsive to gentle touch or voice), 0 (awake and able to calm), +1 (restless and difficult to calm), to +2 (agitated). Although the PSP allows prescribers full freedom to determine the goal SBS score for each patient, all patients in the study had the standard SBS score goal of –1 to 0.

All aspects of the PSP are determined at the clinical discretion of the prescribing intensivist, including the order of infusions used, the actual medications used, dosages, and goal SBS range. Physicians can order between 1 and 4 sedation infusions, with designation by the prescriber on desired sequence for the initial and subsequent medications. Nurses then titrate the sedation infusions within defined parameters to

achieve the designated SBS score. In addition to any infusions, PRN boluses of opioids, benzodiazepines, and ketamine may be ordered at the prescribers' discretion. The standard infusion choices embedded in the electronic order set are dexmedetomidine, morphine, fentanyl, midazolam, and ketamine. Providers can use any of the standard infusions or select other infusions at their discretion. For ketamine, the standard titration range per the PSP is 0.5 to 2 mg/kg/hr (8.3–33.3 mcg/kg/min), which is the standard dosing range established by the hospital, but dosing can be individualized at the prescriber's discretion.

The study period was defined as 24 hours before the patient was initiated on ketamine continuous infusion until 24 hours after the patient was initiated on ketamine; however, data collection on safety outcomes continued until the point of transfer out of PICU or death. Patients who were initiated on ketamine on day 1 of mechanical ventilation were excluded owing to the lack of data during the 24 hours before ketamine started.

Data Collection. All data for this study were obtained by retrospective querying of the patient's medical record. Demographic data, including age (in months), sex, weight, indication for mechanical ventilation, PICU length of stay, and ventilator days, were collected. The indication for starting ketamine was extracted from the medical records via review of the attending physician's notes. Reasons for initiating ketamine were categorized as one of the following: inadequate sedation as determined by the physician (using a combination of SBS scores and clinical examination), sedation rotation in attempt to give a drug holiday, or indication unclear. The duration and average infusion rate of ketamine for each patient were also recorded, as well as the average daily infusion rate of all continuous infusion sedation medications. To evaluate the effectiveness of the sedative medications, all SBS scores documented in the 24-hour periods before and after initiation of ketamine were collected. The use of PRN doses of adjunctive sedation was also collected. The occurrence of adverse effects was noted, including seizure, self-extubation, hypersalivation requiring treatment, tachyarrhythmia requiring treatment, hypertension requiring treatment, and vasopressor use during sedation. Additionally, iatrogenic withdrawal from any sedation medication, as reported in physician notes, was also recorded.

Outcomes. The primary outcome was the effectiveness of sedation with ketamine as defined by a comparison of the percentage of SBS scores within goal range 24 hours prior to initiation of ketamine, compared with the percentage of SBS scores within goal range 24 hours after the initiation of ketamine. Secondary outcomes included a comparison of the number of PRN doses of sedation medication used in the 24 hours before ketamine initiation with the number of PRN doses of sedation medication used in

the 24 hours after ketamine initiation. Safety endpoints were the incidence of adverse effects including seizure, inadequate sedation resulting in self-extubation, hypersalivation requiring treatment, tachyarrhythmia, hypertension requiring treatment, or vasopressor use.

Data Analysis. Data were descriptively analyzed as frequency, average, and standard deviation. Wilcoxon signed rank tests were used to compare the percentage of SBS scores within goal range prior to initiation of ketamine with the percentage of SBS scores within goal range after the initiation of ketamine as well as to compare the number of PRN doses of sedation medication used in the 24 hours before and after ketamine initiation. A p value of 0.05 was used as a significance level.

Results

During the study period, the PSP was used for 185 pediatric patients undergoing mechanical ventilation (Figure). Of these patients, a total of 32 children (17%) received ketamine continuous infusion. Ten patients were excluded from our analysis owing to ketamine duration of less than 12 hours ($n = 1$) or initiation of ketamine at onset of mechanical ventilation ($n = 9$). Of the 22 patients included for analysis (Table 1), the average age was 41 months and 55% were male. None of the study patients died during their hospitalization. The primary indication for mechanical ventilation was respiratory failure in 68% ($n = 15$) of patients and was related to postoperative care in 27% ($n = 6$). The indication for mechanical ventilation in 1 patient was septic shock. None of the 22 patients had a primary diagnosis of asthma. Twelve patients were initiated on ketamine owing to inadequate sedation on previous regimen as determined by the prescribing physician, 8 patients received ketamine in an attempt to rotate sedation medications, and the reason for ketamine use was unclear for 2 patients. Ketamine was always added as adjunct sedation, as all patients were on at least 2 other sedation medications at the time of ketamine initiation (Table 2). Depending on the rationale for ketamine initiation, ketamine was either added to the patient's existing regimen as an additional sedation medication or served to replace one of the medications in the existing regimen. Ketamine continuous infusion was administered at an average rate of 1.02 ± 0.50 mg/kg/hr with a range of 0.07 to 2.0 mg/kg/hr. Most patients were dosed within the PSP's standard range of 0.5 to 2 mg/kg/hr with 5 patients initiating at lower doses owing to prescriber's clinical decision. The duration of ketamine was 65.7 ± 41.0 hours, with a range of 19 to 153 hours.

SBS scores cannot be reliably used in patients receiving neuromuscular blocking medications, therefore 4 patients receiving continuous infusion neuromuscular blockers were not included in the primary outcome owing to lack of SBS scores. In the 24-hour period before initiation of ketamine infusion, $79.3\% \pm 18.7\%$ of SBS scores were within the targeted range of 0 to -1, and in

Figure. Flow diagram with inclusion and exclusion of patients receiving ketamine

the 24-hour period after ketamine was initiated, $79.6\% \pm 20.1\%$ of SBS scores were within the targeted range ($p = 0.78$) (Table 3). The number of PRN sedation doses required was 12.0 ± 6.8 in the 24-hour period before ketamine initiation and 10.7 ± 7.8 in the 24-hour period following ketamine initiation ($p = 0.34$). PRN sedation doses included any bolus dose of opioid, benzodiazepine, or ketamine. A subgroup analysis of the 12 patients started on ketamine to address inadequate sedation showed $73.7\% \pm 20.8\%$ of SBS scores within goal range in the 24 hours before ketamine use, compared to $80.5\% \pm 22.1\%$ of SBS scores in the 24 hours after ketamine was initiated ($p = 0.13$). Among this subgroup, patients required 13.9 ± 6.1 PRN sedation doses in the 24-hour period prior to ketamine and 11.2 ± 7.2 in the 24-hour period after ketamine initiation ($p = 0.34$).

The incidence of adverse effects possibly attributed to ketamine was also reviewed. None of the study patients experienced a seizure during ketamine sedation. No patients experienced self-extubation. Hypersalivation requiring pharmacologic treatment did not occur in

Table 1. Patient Characteristics and Reason for Ketamine Initiation (n = 22)

Age, mo, mean $\pm$ SD (range)	41.17 $\pm$ 41.42 (1–150)
Weight, kg, mean $\pm$ SD (range)	15.06 $\pm$ 8.32 (5.20–34.50)
Male sex, n (%)	12 (55)
Indication for mechanical ventilation, n (%)	
Respiratory failure	15 (68)
Postoperative	6 (27)
Septic shock	1 (5)
Average duration of intubation, days, mean $\pm$ SD (range)	8.67 $\pm$ 4.05 (2–18)
Average PICU length of stay, days, mean $\pm$ SD (range)	13.9 $\pm$ 8.48 (4–36)
Reason for ketamine initiation, n (%)	
Inadequate sedation	12 (55)
Rotation of sedation agent	8 (36)
No reason provided	2 (9)

PICU, pediatric intensive care unit

any patient. Tachyarrhythmia or hypertension requiring treatment was also not noted in any patient during ketamine sedation. Eight patients were being treated with a vasopressor at the time of ketamine initiation. Of these 8 patients, 4 were able to wean or stop the vasopressor medication within 12 hours of starting ketamine. No patients required vasopressor initiation in the 12 hours following ketamine initiation. Eighteen of the 22 patients experienced iatrogenic withdrawal from sedation medications.

Discussion

We report the use of ketamine continuous infusion in 22 mechanically ventilated pediatric patients, examining the effectiveness of sedation as well as the incidence of adverse effects. Ketamine use resulted in no difference in SBS scores before and after ketamine initiation and no difference in the use of bolus sedation medications after ketamine was started. In the subset of patient where ketamine was added owing to inadequate sedation, patients experienced improved sedation scores as well as an overall decrease in PRN sedative use; however, this was not statistically significant. Additionally, there were no adverse effects from ketamine noted in our study population.

Although ketamine is widely used for anesthesia and procedural sedation in pediatrics, its use as a sedative infusion for a broad range of PICU patients is not well described in the literature. Tobias et al¹⁰ first described the use of ketamine continuous infusion to successfully provide sedation and analgesia to 5 critically ill children. Later, Hartvig et al¹¹ described a study of 10 children who received ketamine continuous infusion after cardiac surgery with acceptable analgesia and sedation. Similar to these reports, our study demonstrated effective sedation and analgesia for critically ill children.

Golding and colleagues⁸ reviewed ketamine continuous infusion use in critically ill children. When used specifically for sedation, they described that a total of

6 patients in 2 published case reports had received ketamine for up to 96 hours with effective sedation and no adverse effects. When including ketamine use for indications of withdrawal or bronchospasm, they reported that 74 patients in 3 studies and 8 case reports had received 0.2 to 3.6 mg/kg/hr. Compared to the review of Golding et al,⁸ we also demonstrated effective sedation, the absence of adverse effects, and a similar ketamine dosage range and duration.

Neunhoeffter et al¹² recently reported that 32 mechanically ventilated children received ketamine as part of a sedation drug rotation protocol to minimize opioid tolerance. Ketamine was administered at a median dose of 4 mg/kg/hr (range, 1.8–6 mg/kg/hr) and resulted in a reduction of fentanyl use from 4.15 mcg/kg/hr before ketamine to 2.9 mcg/kg/hr after ketamine ($p < 0.001$) and an improvement in COMFORT-B score (16 vs. 14.5, $p < 0.001$). The doses reported by Neunhoeffter et al¹² are larger than those used in our study (1.02 ± 0.50 mg/kg/hr; range, 0.07–2.0 mg/kg/hr), and though our study was not intended to evaluate opioid tolerance, we are encouraged by this report of the beneficial effects of ketamine. While not a predetermined endpoint of our study, we noted that of the patients on ketamine for the purpose of sedation rotation, at least 1 adjunct sedation infusion was able to be stopped within 24 hours of ketamine initiation for 5 of these 8 patients (Table 2, patients 13–20).

Ketamine use has been associated with both proconvulsant and anticonvulsant properties.⁴ In this study, no patients receiving ketamine experienced a seizure. Additionally, hypersalivation may occur with ketamine use and is often managed with glycopyrrolate or atropine.¹³ No patients required the use of pharmacotherapy for management of hypersalivation. Hypertension and tachyarrhythmias, potential adverse effects of ketamine, were not noted in any of the patients while on ketamine.

Ikonomidou et al¹⁴ have shown that blockage of NMDA receptors in neonatal rat brain has resulted in

Table 2. Sedation Infusions in Addition to Ketamine

Patient	Age, mo	Diagnosis	Rationale for Ketamine	Average Hourly Infusion Rate* (Over 24 Hours) of Adjunct Sedation on the Day Before Ketamine	Average Hourly Infusion Rate* (Over 24 Hours) of Adjunct Sedation on the Day After Ketamine
1	21	Respiratory failure	Inadequate sedation	— [†] Morphine 0.11 Midazolam 0.1	Dexmedetomidine 0.64 Morphine 0.1 Midazolam 0.1
2	18	Respiratory failure	Inadequate sedation	Dexmedetomidine 0.6 Morphine 0.1 Midazolam 0.11	— Morphine 0.13 Midazolam 0.04
3	18	Respiratory failure	Inadequate sedation	Dexmedetomidine 0.5 Morphine 0.05	Dexmedetomidine 1.2 —
4	7	Respiratory failure	Inadequate sedation	Dexmedetomidine 0.7 Morphine 0.15 —	Dexmedetomidine 1.2 Morphine 0.08 Midazolam 0.13
5	8	Respiratory failure	Inadequate sedation	Dexmedetomidine 0.9 Morphine 0.08 Midazolam 0.1	— Morphine 0.2 Midazolam 0.14
6	1	Respiratory failure	Inadequate sedation	Morphine 0.1 Midazolam 0.2	Morphine 0.08 Midazolam 0.14
7	105	Respiratory failure	Inadequate sedation	Dexmedetomidine 1 Morphine 0.05	Dexmedetomidine 1.2 Morphine 0.15
8	67	Respiratory failure	Inadequate sedation	Dexmedetomidine 1.5 Morphine 0.11 Midazolam 0.15	Dexmedetomidine 1.5 Morphine 0.12 Midazolam 0.12
9	93	Postoperative	Inadequate sedation	Dexmedetomidine 1.2 Morphine 0.15 Midazolam 0.15 —	Dexmedetomidine 1.2 — Midazolam 0.1 Fentanyl 2
10	17	Respiratory failure	Inadequate sedation	Dexmedetomidine 1.2 Morphine 0.1 —	Dexmedetomidine 1.2 Morphine 0.11 Midazolam 0.05
11	16	Postoperative	Inadequate sedation	Dexmedetomidine 1.2 Midazolam 0.07 Fentanyl 5	Dexmedetomidine 1.1 Midazolam 0.08 Fentanyl 7
12	18	Postoperative	Inadequate sedation	— Morphine 0.15 Midazolam 0.15	Dexmedetomidine 0.9 Morphine 0.21 Midazolam 0.2
13	8	Respiratory failure	Rotation of sedation agents	Dexmedetomidine 1.2 Morphine 0.05	Dexmedetomidine 1.2 —
14	55	Respiratory failure	Rotation of sedation agents	Dexmedetomidine 0.9 Morphine 0.14 Midazolam 0.09	— Morphine 0.17 Midazolam 0.12
15	34	Postoperative	Rotation of sedation agents	Dexmedetomidine 1.2 Midazolam 0.05	Dexmedetomidine 1 Midazolam 0.1
16	49	Shock	Rotation of sedation agents	Morphine 0.1 Midazolam 0.05	Morphine 0.1 Midazolam 0.07
17	56	Respiratory failure	Rotation of sedation agents	Dexmedetomidine 0.5 Morphine 0.18 Midazolam 0.12	Dexmedetomidine 1.14 Morphine 0.05 —

* Dosing units: dexmedetomidine, mcg/kg/hr; fentanyl, mcg/kg/hr; midazolam, mg/kg/hr; morphine, mg/kg/hr.

[†] — dexmedetomidine, morphine, midazolam, or fentanyl not administered.

Table 2. Sedation Infusions in Addition to Ketamine (*cont.*)

Patient	Age, mo	Diagnosis	Rationale for Ketamine	Average Hourly Infusion Rate* (Over 24 Hours) of Adjunct Sedation on the Day Before Ketamine	Average Hourly Infusion Rate* (Over 24 Hours) of Adjunct Sedation on the Day After Ketamine
18	150	Postoperative	Rotation of sedation agents	Dexmedetomidine 0.7 Morphine 0.02	— —
19	35	Respiratory failure	Rotation of sedation agents	Dexmedetomidine 0.6 Midazolam 0.08	— —
20	11	Respiratory failure	Rotation of sedation agents	Dexmedetomidine 1 Morphine 0.08 —	Dexmedetomidine 1.2 — Fentanyl 2.3
21	3	Respiratory failure	Unable to determine	Dexmedetomidine 1.2 Morphine 0.07 —	— Morphine 0.15 Midazolam 0.15
22	116	Postoperative	Unable to determine	Fentanyl 2.8 Midazolam 0.06 —	Fentanyl 3.5 — Dexmedetomidine 0.5

* Dosing units: dexmedetomidine, mcg/kg/hr; fentanyl, mcg/kg/hr; midazolam, mg/kg/hr; morphine, mg/kg/hr.

† — dexmedetomidine, morphine, midazolam, or fentanyl not administered.

widespread apoptosis and neuronal cell death. While data are mostly derived from animal models, ketamine has also been shown to alter neurogenesis by affecting proliferation and cellular differentiation,¹⁵ though further studies are needed to evaluate this concern. These potential effects on the developing brain are not unique to ketamine, as other sedation medications used in children have similar concerns.^{16–18} Conversely, a study investigating short-term neurodevelopmental effects of ketamine in infants undergoing cardiac surgery and bypass did not show significant difference in Bayley scales of infant development-II scores.¹⁹ We also note that ketamine may have some neuroprotective properties in traumatic brain injury. Hertle et al²⁰ showed decreased cortical spreading depolarization, which can further reduce neurological damage with ketamine compared to other sedative agents. Prospective studies investigating long-term neurological outcomes of sedatives and analgesics in neonates and infants would provide further insight to this topic.

There were several limitations to this study. The study was single center and had a small number of subjects. We compared SBS scores before ketamine initiation to SBS scores after ketamine initiation. Any changes in level of sedation could be affected by many different variables, making it difficult to attribute sedation level directly to ketamine. The indication for ketamine was

variable, with some patients starting ketamine as part of an attempt to rotate sedation medications to decrease withdrawal and some patients starting ketamine owing to inadequate sedation. All patients were on multiple sedation medications and titration of these infusions continued after initiation of ketamine, which further limits the ability to isolate ketamine's effects on adequate sedation. In particular, our patient cohort, like other intubated PICU patients, frequently required multiple sedation medications, making it difficult to definitively elucidate the effects of ketamine. Similarly, for patients with inadequate sedation, it is typical to add more than 1 medication in an effort to achieve adequate sedation, again impeding the ability to isolate the effects of ketamine. A review of individual regimens of patients with inadequate sedation (Table 2, patients 1–12) reveals that 8 patients had only the addition of ketamine, whereas 4 patients required additional sedation infusions of dexmedetomidine or midazolam. While it is difficult to conclude the effects of ketamine with multiple sedation variables, our data reflect the real-life challenges of sedating intubated pediatric patients.

There is a potential concern regarding withdrawal following the prolonged use of ketamine infusions. While 18 of the 22 patients experienced iatrogenic withdrawal, it is difficult to ascertain whether their symptoms were from ketamine withdrawal or from other sedation

Table 3. Percentage of SBS Scores Within Targeted Range (n=18) and Number of Sedation Boluses (n=22)

	24-Hour Period Before Ketamine	24-Hour Period After Ketamine Initiation	p value
% of SBS scores within targeted range, mean $\pm$ SD	79.3 $\pm$ 18.7	79.6 $\pm$ 20.1	0.78
Number of sedation boluses per patient, mean $\pm$ SD	12.0 $\pm$ 6.8	10.7 $\pm$ 7.8	0.34

SBS, State Behavioral Scale

medications these patients received. It is common for patients to exhibit withdrawal symptoms from opioids, benzodiazepines, and dexmedetomidine, which were used as concomitant sedation. We did not look specifically for emergence phenomenon in this study, as our experience is that we do not see this when using ketamine as part of the PSP. We suspect that this is likely because our typical clinical practice is to discontinue ketamine while patients are still receiving other infusions, which may mask any emergence phenomenon.

In our population of mechanically intubated pediatric patients, the addition of ketamine continuous infusion as part of a multidrug sedation regimen was associated with no difference in level of sedation or the need for bolus sedation medication. Based on the ability to achieve target SBS scores, the sedation regimen after the addition of ketamine was at least as effective as the patients' previous sedation regimen. While not statistically significant, improved sedation with ketamine was noted in those patients with inadequate sedation scores prior to starting ketamine. There were no reported adverse effects during ketamine infusion. Ketamine is an alternative agent for pediatric patients requiring sedation and analgesia during mechanical ventilation, but further randomized studies comparing ketamine to standard sedation methods are needed to better define ketamine's role in PICU sedation.

ARTICLE INFORMATION

Affiliations Sanford Children's Hospital (ALH, GO, LL, CL, HM), Sioux Falls, South Dakota; South Dakota State University College of Pharmacy and Allied Health Professions (ALH), Brookings, South Dakota; Auburn University Harrison School of Pharmacy (SN), Auburn, Alabama; University of South Dakota Sanford School of Medicine (GO), Sioux Falls, SD; Yale University School of Medicine, Department of Pediatrics (SAL), New Haven, Connecticut.

Correspondence Saquib A. Lakhani, MD; saquib.lakhani@yale.edu

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