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Ketamine for Primary Analgosedation in Critically III Surgery and Trauma Patients Requiring Mechanical Ventilation

OBJECTIVES: Evaluate effectiveness and safety outcomes associated with the use of ketamine for primary analgosedation in the surgical/trauma ICU setting.

DESIGN: Retrospective cohort study.

SETTING: Academic medical center in Minnesota.

PATIENTS: Patients admitted to the surgical ICU between 2015 and 2019 requiring mechanical ventilation and meeting one of three definitions for ketamine primary analgosedation were included: 1) no concomitant opioid infusion, 2) ketamine monotherapy for greater than or equal to 6 hours with subsequent opioid infusion, or 3) ketamine initiated concomitantly or within 4 hours of opioid and total opioid duration less than 4 hours.

INTERVENTIONS: None.

MEASUREMENTS: Use of ketamine, analgesics, and sedatives were evaluated. Pain, sedation, and delirium assessments immediately before and during ketamine infusion were collected and compared with reported goals. Concomitant analgesics, sedatives, and psychotropics were recorded. Reported failures due to ineffectiveness and toxicity were collected.

MAIN RESULTS: Of 164 included patients, 88% never received a concomitant opioid infusion (primary analgosedation definition 1), 12% met alternative criteria for primary analgosedation (definitions 2 and 3). A majority, 68%, were surgical admissions and mean Acute Physiology and Chronic Health Evaluation III score was 90 (\pm 30). Median mechanical ventilation duration was 2.5 days (1.1–4.5) and ICU length of stay of 4.9 days (3–8). The median ketamine infusion dose and duration were 0.18 mg/kg/hr (0.1–0.3) and 30 hours (15.1–51.8). Concomitant infusions of propofol and dexmedetomidine were administered in 49% and 29% of patients, respectively. During ketamine infusion, the median percent of total pain scores at goal was 62% (33–96%), while 64% (37–91%) of Richmond Agitation Sedation Scale scores were at goal, and 47% of patients were Confusion Assessment Method-ICU positive during the ketamine infusion. Hallucinations were documented in 14% of patients and ketamine failure occurred in 11% of patients.

CONCLUSIONS: Ketamine may be an effective primary analgosedation option in intubated surgical ICU patients, but prospective randomized studies are needed to evaluate this strategy.

KEYWORDS: analgosedation; ketamine; surgery; trauma

ain, agitation, and delirium are exceedingly common in critically ill patients requiring mechanical ventilation and effective management of these intertwined conditions is a fundamental component of ICU practice (1). The evidence focused on these issues has evolved considerably in the last two decades, leading to an emphasis on systematic assessment, an

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KEY POINTS

Question: The objective was to describe the use of ketamine as a primary analgosedation agent in an intubated surgical-trauma population.

Findings: In this retrospective, cohort of critically ill intubated surgical-trauma patients ketamine was used as the primary analgosedation agent in 164 patients at a median dose of approximately 0.2 mg/kg/hr. The percent of pain and sedation scores at goal were both greater than 60%, and nearly half the population were considered Confusion Assessment Method-ICU positive at some point during the ketamine infusion.

Meaning: A ketamine infusion as primary analgosedation is feasible and appears effective in an intubated critically ill surgical-trauma population.

analgosedation (or analgesia-first) approach, targeting light sedation, and a preference toward nonbenzodiazepine sedatives (1, 2). With respect to analgosedation in the ICU, pain is treated before sedative initiation and the analgesic may also be used to achieve the sedation goal; current guidelines still recommend opioids as the mainstay of therapy (2). Although effective, the toxicities and limitations of opioids are well recognized. Particularly in the trauma and general surgical ICU population, who are expected to have pain requiring treatment, multimodal therapy is suggested to reduce opioid requirements despite minimal prospective evaluation in this population (3). Adding to the significance of this issue is the opioid epidemic, causing providers and institutions to consider multiple practice changes and reduce opioid exposure wherever possible (4).

Ketamine, an agent with both analgesic and sedative properties, represents an alternative analgosedation agent with the potential to manage pain and agitation while minimizing opioid and sedative requirements (5–7). Other differentiating features include a lack of respiratory depression at subanesthetic doses and positive effects on blood pressure (5, 8). Potential adverse effects include dissociative effects, delirium, and increased respiratory secretions (5, 8). This agent acts primarily through *N*-methyl-D-aspartate-antagonism and as an opioid receptor agonist, with numerous additional targets that may be involved in the observed effects (8).

Historically, ketamine has been used effectively in short durations to facilitate painful procedures in many settings (including the ICU), taking advantage of its well-known analgosedation properties (6, 7). Although the use of a ketamine infusion as a primary agent to manage pain and agitation in the critically ill population requiring mechanical ventilation may seem logical, the available evidence is mostly limited to retrospective evaluations of adjunctive ketamine use (5-7). Such studies have reported reduced opioid and sedative requirements following ketamine initiation while achieving pain and sedation goals, but these studies have not included a control group and are inconclusive (9-11). Guidelines do not provide recommendations regarding the potential use of ketamine as an analgosedation agent, although they do suggest consideration for low-dose adjunctive ketamine in postoperative ICU patients based on one trial of abdominal surgery patients (2).

Given the known effects of ketamine and the desire to minimize opioid exposure among critically patients requiring mechanical ventilation, a strategy in which ketamine is used as a first-line analgosedation agent in the ICU merits consideration. The objective of this study was to describe the utilization of ketamine as a primary analgosedation agent in surgical-trauma ICU patients including an evaluation of its effectiveness and safety.

MATERIALS AND METHODS

Study Design, Patient Population, and Setting

This was a single-center retrospective study performed at a large, quaternary-care academic hospital that serves as a level 1 trauma center.

The mayo clinic institutional review board (IRB) reviewed and approved the study protocol with a waiver of informed consent due to the minimal risk nature of the study on November 22, 2022 under the title of "Comparison of continuous infusion ketamine versus opioids for primary analgosedation in mechanically ventilated trauma ICU patients" and IRB ID of 22-010481. All procedures and protocols were in accordance with ethical standards on human experimentation and with the Helsinki Declaration of 1975. Adult patients (\geq 18 yr) were included if they were admitted

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between January 1, 2015 and November 15, 2019 to the surgical/trauma ICU, required mechanical ventilation, and received ketamine for at least 6 hours as primary analgosedation. Primary ketamine analgosedation was defined in one of three ways: 1) ketamine infusion used for greater than or equal to 6 hours with no opioid infusion used, 2) ketamine infusion was used as the only analgesic infusion for greater than or equal to 6 hours and subsequently an opioid infusion was initiated, and 3) ketamine was initiated either concomitantly or within 4 hours of an initial opioid infusion and the total opioid infusion duration was less than 4 hours. Exclusion criteria included receipt of ketamine for status epilepticus or refractory pain management prescribed by the pain service, receipt of fentanyl or hydromorphone infusions for greater than or equal to 4 hours before the initiation of the ketamine infusion, and lack of authorization for research in the State of Minnesota.

In the surgical-trauma ICU, ketamine infusions are managed by the ICU provider staff, which is comprised of surgeons, surgical ICU fellows, advanced practice providers, and surgical residents. There is no formal protocol for initial dosing and/or titration parameters for the ketamine infusion, but the approach of using ketamine for primary analgosedation is very common across providers, with dosing adjustments at the discretion of the critical care staff with input from the interdisciplinary team, including pharmacists, nurses, and respiratory therapists. Multimodal analgesic therapy is common, with nearly all patients receiving scheduled acetaminophen, selective use of gabapentinoids and very limited use of nonsteroidal antiinflammatory drugs.

Data Collection and Outcomes

Data were collected through both electronic query and manual chart review, including baseline demographics, admitting diagnosis, medical history of a psychiatric disorder (anxiety, depression, bipolar, schizophrenia, and obsessive-compulsive disorder), presence of antipsychotic, benzodiazepine, or opioid use based on outpatient prescription records from the prior 90 days, and history of substance abuse. History of substance abuse (alcohol, cocaine, amphetamines, opioids) was determined from provider documentation and/or positive toxicology screen at admission.

All pain, sedation, and delirium assessments immediately before and during ketamine infusion were recorded. The percentage of pain and sedation scores at goal during the ketamine infusion were determined to evaluate effectiveness. For pain assessment, the Critical Care Pain Observation Tool (CPOT) and Numeric Rating Scale (NRS) were both used, depending on the patient's ability to communicate. The goal pain scores were defined as a CPOT less than 3 and a NRS of less than 4 (of 10). For level of sedation, the Richmond Agitation Sedation Scale (RASS) was used, and each patient's RASS goal was recorded. The default RASS goal in the unit is 0 to -2 for most patients, but critical care staff can establish patient-specific goals, and these were reviewed via manual chart review and recorded. Delirium was assessed using the Confusion Assessment Method for the ICU (CAM-ICU) at a minimum once a day but frequently more often. Ketamine dose and duration were collected, as well as the occurrence of ketamine failure or documented adverse effects. Failure was defined as discontinuation due to either perceived ineffectiveness or concern for toxicity as documented in the critical care provider note. Ketamine toxicity was evaluated through manual chart review and included hemodynamic effects (i.e., tachycardia, hypotension, or hypertension), increased airway secretions, psychiatric reactions (i.e., hallucinations, agitation), or any other documented concern.

Sedative (propofol, dexmedetomidine, midazolam, lorazepam), analgesic (fentanyl, hydromorphone, oxycodone, morphine, tramadol, pregabalin, gabapentin), and antipsychotic (haloperidol, quetiapine, olanzapine, ziprasidone) administration during ketamine infusion was recorded. Enteral benzodiazepines and antipsychotics were recorded if they were initiated in the ICU and not resumed as part of a patient's prior outpatient regimen. Other clinical outcomes of interest included duration of mechanical ventilation, ICU and hospital length of stay (LOS), and hospital mortality.

Statistical Analysis

Descriptive statistics were used to report data. Data are presented as median and interquartile range (IQR) or mean and sD, as appropriate. Percentage of pain or sedation scores at goal were determined by the number of documented scores at their goal divided by the total reported scores during the ketamine infusion, multiplied by 100. Univariate logistic regression was used to assess if any patient or clinical characteristics were associated with ketamine failure. Due to a limited number of events, we were unable to do a multivariable logistic regression model.

RESULTS

A total of 252 patients were screened and 164 patients met our criteria for inclusion and were evaluated. The vast majority (88%, n = 144) never received a concomitant opioid infusion during their ICU stay (analgosedation definition 1); 12% (n = 20) met alternative criteria for primary analgosedation (definition 2 or 3). Baseline demographics are reported in Table 1. The majority of patients were surgical admissions (68%) with the remainder admitted for trauma, and the mean Acute Physiology and Chronic Health Evaluation III score was 90 (sp ±30). Documented psychiatric illness was present in 27% of patients, primarily driven by depression and anxiety. A history of substance abuse was present in 30.9% of patients. Over 30% used an opioid, benzodiazepine or gabapentinoid before admission.

Ketamine Dosing

Ketamine was used for a median duration of 29.8 hours (IQR 15.1–51.8) and the median infusion rate was 0.18 mg/kg/hr (IQR 0.1–0.3), **Table 2**. When ketamine was used as the sole infusion (no concomitant analgesic or sedative infusion, n = 54), the median infusion rate was 0.14 mg/kg/hr (IQR 0.1–0.2). When ketamine was paired with a continuous sedative infusion (benzodiazepines, dexmedetomidine, propofol) (n = 105), the median dose was 0.2 mg/kg/hr (IQR 0.1–0.3) and when paired with a continuous opioid infusion (n = 20) the median infusion rate was 0.28 mg/kg/hr (IQR 0.1–0.4) (**Table S1**, http://links.lww.com/CCX/B300).

Concomitant Analgesic, Sedative, and Antipsychotic Utilization

A concomitant opioid infusion was administered in only 12% (n = 20) of patients; for 14 patients the opioid infusion was initiated after greater than or equal to 6 hours of ketamine monotherapy, and in six patients the opioid was administered within the first 4 hours of ketamine infusion but was used for less than 4 hours duration. Fentanyl was used in 18 patients (11%) for a median duration of 6.7 hours (IQR 1.5–26.1) and hydromorphone in 3 patients (2%) for 23.8 hours (IQR 0.7–43.1). Intermittent doses of opioids were administered to 80% of patients, who received a median of six doses (IQR 3–12). The median total oral morphine equivalent exposure among patients receiving intermittent opiates, including IV and enteral doses, was 96 mg (IQR 36–235).

A continuous sedative infusion was concomitantly administered in 64% of patients; propofol was used in 80 patients (49%) for a median duration of 3.5 hours (IQR 1.4–10.1), dexmedetomidine in 48 (29%) patients for a median duration of 4.2 hours (IQR 0.8–21.4), and midazolam in 1 (1%) patient for 0.75 hours. Dosing for sedative agents is reported Supplement Table S1 (http://links.lww.com/CCX/B300).

Either gabapentin or pregabalin was administered in 31 patients (19%), receiving a median of three doses (IQR 2–5) during the ketamine infusion; additional details regarding gabapentinoid use can be found in **Table S2** (http://links.lww.com/CCX/B300) New administration of at least one dose of either a benzodiazepine or antipsychotic agent occurred in 63 patients (25%). Forty-seven patients (19%) received a new benzodiazepine, and 16 patients (6%) received a new antipsychotic. There were no documented toxicities of increased secretions. Two patients had hemodynamic alterations, one of which was tachycardia and the other persistent hypertension.

Clinical Outcomes

During the ketamine infusion, 62% (IQR 33–96%) of documented pain scores were within the goal, whether measured by CPOT (median 2 [IQR 0–4]) or NRS (median 3 [IQR 0–5]) (**Table 3**). The mean level of sedation during ketamine was a RASS score of -1 (±1.5) and 64% (37–91) of RASS scores were at goal. Delirium, as determined by the presence of at least one positive CAM-ICU score of those with CAM-ICU assessment, occurred in 61 patients of 131 (47%).

Ketamine failure resulting in discontinuation occurred in 18 patients (11%); failure was due to perceived ineffectiveness in 11 patients and toxicity in 11 patients, with 4 patients experiencing both. Univariate analysis failed to identify any predictors of ketamine failure (**Table S3**, http://links.lww.com/CCX/B300). Hallucinations and agitation during ketamine, not necessarily resulting in discontinuation, occurred in 4 and 18 patients, respectively.

TABLE 1.Baseline Demographics

Baseline Demographics	164 Patients
Age, mean (sp)	62.6 (± 17.8)
Male gender	96 (58.5%)
Weight (ICU admit), mean (SD)	91.5 (± 29.6)
Race	
White	135 (82.3%)
Black or African American	6 (3.7%)
Other	11 (6.7%)
Unknown	12 (7.3%)
Admission diagnosis	
Surgical	111(68%)
Trauma	53(32%)
Acute Physiology and Chronic Health Evaluation III, mean (sp)	90 (±30)
Psychiatric history ^a	44(26.8%)
Anxiety	23 (13.9%)
Depression	35 (21.2%)
Bipolar	4 (2.4%)
Schizophrenia	1 (0.6%)
Obsessive-compulsive disorder	1 (0.6%)
Outpatient/chronic medication use ^b	
Opioid analgesic	50 (30.3%)
Gabapentin or pregabalin	19 (11.5%)
Benzodiazepine	16 (9.6%)
Antipsychotic	8 (5%)
History of substance abuse ^c	51 (30.9%)
Documented	23 (13.9%)
Laboratory confirmed	33 (20%)
Primary analgosedation use/category	
No concomitant opioid infusion	144 (88%)
Ketamine monotherapy for \geq 6 hr with subsequent opioid infusion	14 (9%)
Ketamine initiated either concomitantly or within 4 hr of opioid and total opioid $<$ 4 hr	6 (3%)
Richmond Agitation Sedation Scale score before ketamine initiation, mean (sp) ^d	-1.6 (± 2)
Pain Score before ketamine initiation, median (IQR) ^e	
Critical Care Pain Observation Tool	1 (0-4)
Numeric Rating Scale	4 (0-7)
Confusion Assessment Method-ICU Positive before Ketamine Initiation	
Positive	31 (199%)
Negative	52 (32%)
Not available	81 (49%)

^aWithin 5 yr of admission.

^bOn outpatient medication list within 90 from admission.

^cDocumented within 5 yr of admission.

 $^{d}n = 137$ patients had Richmond Agitation Sedation Scale assessments before ketamine initiation.

 $^{\circ}n = 110$ patients had pain assessments before ketamine initiation.

TABLE 2.Ketamine Dosing and ConcomitantAnalgesia and Sedative Usage

Ketamine Dosing and Concomitant Analgesia and Sedative Usage

Ketamine use $(n = 164)$	
Total dose, median (IQR)	411.9mg (156.6–1087.9)
Infusion duration, median (IQR)	29.8 hours (15.1–51.8)
Infusion rate (mg/kg/hr), median (IQR)	0.18 mg/kg/hr (0.1-0.3)
Ketamine used as only infusion	54 (33%)
Dose (mg/kg/hr), median (IQR)	0.14 mg/kg/hr (0.1–0.2)
Received concomitant sedative infusion	105 (64%)
Propofol	80 (49%)
Dexmedetomidine	48 (29%)
Midazolam	1 (1%)
Received concomitant opioid infusion	n = 20 (12%)
Fentanyl	18 (11%)
Hydromorphone	3 (2%)
Received intermittent as needed opioid doses	131 (80%)
Administration of new benzodi- azepines during ICU stay ^a	47 (29%)
Administration of new antipsychotics during ICU stay ^a	16 (10%)

IQR = interquartile range.

^aNew IV/IM/PO intermittent administration, not continuous infusion.

For the overall population, the median duration of mechanical ventilation was 2.5 days (IQR 1.1–4.5). Patients had a median ICU LOS of 4.9 days (IQR 3–8), and hospital LOS was 15.9 days (IQR 9.9–24.9). In-hospital mortality occurred in 24 of patients (15%).

DISCUSSION

We report on the unique application of ketamine as first-line analgosedation in a large cohort of mechanically ventilated surgical-trauma ICU patients, observing that the vast majority of patients were able to achieve pain management goals with a relatively low-dose ketamine infusion and only as-needed doses of opioids. These findings suggest a strategy using ketamine as a

TABLE 3.Clinical Outcomes

Analgosedation	outcomes
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RASSª, mean (SD)	-1 (±1.5)
Percent of RASS scores within goal, median (IQR)	64% (37–91)
Any confusion assessment method- ICU+ ^b during ketamine infusion	61 patients (47%)
Pain scores ^₀	
CPOT, median (IQR)	2 (0-4)
NRS, median (IQR)	3 (0–5)
Pain scores within goal ^d , median% (IQR)	62% (33–96%)
CPOT, median% (IQR)	67% (37.5–87.5%)
NRS, median% (IQR)	63% (25–100%)
Documented ketamine failure	18 (11%)
Due to perceived ineffectiveness	11 (6.7%)
Due to perceived toxicity	11 (6.7%)
Documented hallucinations or agitation	22 (14%)
General outcomes	
Duration of mechanical ventilation, median (IQR)	2.5 d (1.1–4.5)
ICU length of stay, median (IQR)	4.9 d (3–8)
Hospital length of stay, median (IQR)	15.9 d (9.9–24.9)
In-hospital mortality, <i>n</i> (%)	24 (15%)

CPOT = Critical Care Pain Observation Tool, IQR = interquartile range, NRS = Numeric Rating Scale, RASS = Richmond Agitation Sedation Scale.

n = 160 patients had RASS assessments documented during ketamine infusion.

 ${}^{b}n = 131$ patients had Confusion Assessment Method-ICU assessments documented during ketamine infusion.

 $^{c}n = 144$ patients had pain assessments (83 CPOT and 129 NRS) documented during ketamine infusion.

^dWithin goal pain scores are CPOT < 3 and NRS < 4.

primary analgosedation agent may be a safe and effective option in surgical-trauma ICU (SICU) patients with potential to significantly reduce opioid exposure. This represents an expansion of the uses of ketamine beyond the adjunctive roles in therapy previously described in similar populations and warrants further investigation.

Multiple previous studies have described outcomes observed among retrospective cohorts of critically ill patients (mostly in the surgical-trauma setting) in which ketamine was used as adjunctive analgosedation

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(6, 7, 12-15). Almost all patients included in these cohorts were receiving sustained (> 24 hr) durations of continuous opioid infusion and a majority were also receiving a sedative infusion before ketamine initiation. Presumably, ketamine was added either to address unmet pain and sedation goals or to reduce opioid and alternative sedative exposure. Generally, these studies have observed significant reductions in opioid and sedative exposure in the 24-48 hours immediately following ketamine initiation, while achievement of pain and sedation goals were maintained or improved. Groetzinger et al (14) reported that one-half of patients had at least one "sedative agent" discontinued following ketamine initiation, including discontinuation of fentanyl infusion in ~13% of patients receiving this at baseline. Similarly, Bucheit et al (15) reported fentanyl discontinuation in over half of patients following ketamine initiation. A recent multicenter observational study including 390 ICU patients receiving ketamine infusions explored a broad range of indications (analgesia/sedation in 92%) and associated outcomes (16). Among those receiving ketamine for analgesia/sedation, the outcomes observed were in alignment with previous retrospective studies of adjunctive ketamine use. Collectively, these studies suggest that ketamine use may result in reduced requirements for opioids and alternative sedatives while achieving pain and sedation goals. Given the consistency of these findings, it begs the question as to whether upstream use of ketamine as a primary analgosedation agent may have a role.

We identified one previous study, which retrospectively compared 22 patients receiving continuous infusions of ketamine and propofol to 24 patients receiving fentanyl and propofol; all patients were mechanically ventilated in a surgical-trauma ICU (17). Opioid utilization during the period of mechanical ventilation was significantly reduced in the ketamine/propofol group. The proportion of time at goal pain scores was statistically significantly lower in the ketamine/propofol group (78% vs. 89%), whereas time at goal level of sedation was not significantly different between groups.

In our present study, 88% of mechanically ventilated SICU patients receiving ketamine for primary analgosedation never required an opioid infusion during their ICU stay. Additionally, approximately one-third received ketamine as the only analgesic or sedative infusion; for the patients that received a concomitant sedative infusion, the average durations were short (< 4.5 hr), and doses were relatively low. During ketamine infusion, approximately 60% of pain and sedation scores were within the goal range, which is generally consistent with findings from previous studies involving ketamine as well as randomized trials involving dexmedetomidine and propofol for ICU sedation (18, 19). Of note, the ketamine doses used in our study were relatively low, representing the lower end of those reported in studies exploring adjunctive ketamine use.

Respective to toxicity, chief concerns include dissociative effects, potential for increased delirium, increased airway secretions, and hemodynamic alterations. In our cohort, ketamine was discontinued due to perceived toxicity in 7% of patients which is very similar to the rates of discontinuation due to an adverse effect observed by Groetzinger et al (7.7%) and Groth et al (5.7%) (14, 16). Hallucinations or agitation were documented to occur in 2% and 11%, respectively. Delirium occurred in almost half of patients and antipsychotics were newly started in 16 (10%). Due to the lack of a comparator group in previous studies as well as ours, it is difficult to evaluate safety outcomes, and this remains an important priority for future research focusing on ketamine in the ICU.

Ketamine failure, due to either perceived ineffectiveness or toxicity, was observed in 11% of patients. We performed an analysis to explore factors that may predict ketamine failure but did not identify any independent factors. Taken together, these findings suggest ketamine has the potential to effectively replace an opioid infusion as the primary analgosedation agent for a proportion of critical ill surgical-trauma patients.

The primary implication of this study is that use of ketamine as a primary analgosedation agent in mechanically ventilated ICU patients warrants further investigation. Our findings suggest that use of a low-dose ketamine infusion with as-needed doses of opioids may represent an effective strategy to meet pain and sedation goals for many surgical-trauma patients. Previous studies provide support for further study of adjunctive ketamine use in the ICU. However, prospective trials directly comparing ketamine-based to nonketaminebased strategies are necessary to understand how both efficacy and safety outcomes in the ICU are impacted. Amidst the significant concern for any unnecessary opioid exposure, it is also important to explore any potential impact on long-term use of analgesics or sedatives with addiction potential.

Strengths of this study include its relatively large sample size and a robust evaluation of the available pain, sedation, and delirium measures. A primary limitation is the lack of a comparator group (similar to previous studies exploring ketamine in the ICU), which limits our ability to draw any conclusions about effectiveness or safety relative to nonketamine-based strategies. Additionally, the population was limited to mechanically ventilated surgical-trauma patients, and as such our findings may not be broadly applicable to other ICU populations. Finally, the use of ketamine was not standardized either in the criteria for use or the approach to ketamine dosing and adjustment of other agents; this may lead to selection bias in the patients who received ketamine. However, we note that this practice has been used in this ICU for nearly a decade across providers in the participating ICU, and medication adjustments according to clinician discretion is a component of clinical practice.

CONCLUSIONS

Our findings suggest that use of ketamine for primary analgosedation agent may be an effective strategy in mechanically ventilated surgical-trauma ICU patients. This unique approach has the potential to reduce opioid exposure while achieving pain and sedation management goals. However, further investigation including prospective, randomized trials of ketamineand nonketamine-based strategies are necessary to assess both efficacy and safety outcomes.

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