Low-Dose Ketamine Infusion to Decrease Postoperative Delirium for Spinal Fusion Patients

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Purpose: *The primary aim of this project was to decrease the incidence of postoperative delirium after spine surgery.*
Design: *A prospective preimplementation and postimplementation design was used.*
Methods: *A reduced dose ketamine protocol was implemented for adult patients undergoing elective spinal fusion surgery. Thirty patients were assessed at five time points for the presence of postoperative delirium in the postanesthesia care unit (PACU) using the 3-Minute Diagnostic Interview for Confusion Assessment Method Defined Delirium tool and opioid requirements were compared.*
Findings: *A statistical difference was noted between two groups in the incidence of delirium at three of five time points: on arrival to the PACU, and at 60 and 90 minutes after arrival to the PACU.*
Conclusions: *This pilot study establishes groundwork for further studies to investigate if the ketamine dose can decrease the incidence of postoperative delirium in the initial 90 minutes after surgery without decreasing its analgesic effect.*

Keywords: *ketamine, delirium, spinal fusion, 3D-CAM.*

DELIRIUM AFFECTS MORE than 2.3 million hospitalized adults generating up to $150 billion in health care costs annually.[1,2] A meta-analysis reported that delirium occurs in up to 21.3% of spine surgery patients[3] and in 40% of surgical patients aged more than 70 years.[4] Postoperative delirium after spine surgery is associated with an increased hospital length of stay (LOS), higher mortality rates, and increased hospital discharges to skilled nursing facilities when compared with patients who did not exhibit postoperative delirium.[1] Hospital costs associated with postoperative delirium have been shown to increase more than $13,300 per admission.[1] In addition, patients with postoperative delirium demonstrated an increase in adverse complications, poor functional recovery, and decreased cognitive ability.[1]

Review of Literature

Ketamine is commonly used in spine surgery as a nonopioid analgesic, decreasing opioid requirements.[5-7] The American Pain Society recommends

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Conflict of interest: None to report.

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1089-9472/$36.00
https://doi.org/10.1016/j.jopan.2018.11.009

intravenous ketamine as a component of multimodal analgesia in adults undergoing extensive surgery, especially those who are opioid tolerant.[8] Despite the benefits of ketamine, its use can pose significant challenges including emergence delirium, which has occurred in nearly 50% of patients after ketamine administration.[9] Additional manifestations include schizophrenic-like behavior, hallucinations, and altered perceptions.[9] The beneficial and adverse effects of ketamine are dose-related, but optimal dosing of ketamine remains undetermined.[7,10]

The current recommended postoperative opioid-sparing dose of ketamine derived from randomized controlled trials consists of a 0.5 mg/kg bolus followed by a continuous infusion at 2 mcg/kg/min (0.12 mg/kg/h).[5] When ketamine was infused intraoperatively at these dosing parameters, during open renal surgery, there was a significant decrease in reported pain scores and no reported psychiatric side effects.[11] In a prospective, randomized double-blind study of rib fracture patients, low-dose ketamine was continued for 48 hours resulting in decreased pain scores during the first 24 hours and reduced overall intake of oral morphine equivalents.[12] In spinal fusion patients with chronic pain, Kim et al[5] used the same dosing parameters for 48 hours and found a decrease in opioid consumption in the 48-hour postoperative period, without an increase in psychotomimetic disturbances. Low-dose intraoperative ketamine administered at a bolus of 0.15 to 0.5 mg/kg with an infusion of 0.1 to 0.2 mg/kg/min (1.6 to 3.4 mcg/kg/min) is commonly used in a wide range of surgical procedures.[7]

The purpose of this quality improvement (QI) project was to decrease the incidence of postoperative delirium after spine surgery, without sacrificing analgesic control, by modifying the current intraoperative ketamine administration protocol. The project aims included (1) determining the baseline delirium rate after spine surgery, as measured by the 3-Minute Diagnostic Interview for Confusion Assessment Method Defined Delirium (3D-CAM) tool; (2) modifying the current ketamine protocol from 4 to 2 mcg/kg/min, while maintaining the initial loading dose at 0.5 mg/kg; (3) educating anesthesia providers about the protocol change and overseeing its implementation; (4) using the 3D-CAM to measure the incidence of postoperative delirium; and (5) comparing the preopioid and postopioid requirements after implementation.

Materials and Methods

Design, Setting, and Participants

This exploratory pilot QI project used a prospective preimplementation and postimplementation group design with independent samples. It was conducted at a tertiary care, 957-inpatient bed, level I academic trauma center, located in the Southeastern United States. The facility has 51 operating rooms and performs over 1,200 spine surgeries annually. After spine surgery, patients are typically admitted to a neurologic or surgical intensive care unit (ICU), step-down unit, or a dedicated orthopaedic floor. The anesthesia department comprises 80 anesthesiologists and 135 nurse anesthetists facility-wide. Within the department is a "spine team" comprising anesthesia providers who regularly administer anesthesia to spine surgical patients.

A convenience sample of 30 adult patients undergoing thoracolumbar spinal fusion was evaluated: 14 preimplementation and 16 postimplementation. Ethical considerations included formal evaluation using an internal checklist created by the Institutional Review Board and School of Nursing that determined the project to be QI rather than human subject's research; therefore, this project did not require Institutional Review Board approval. Patients aged 18 years or older, and American Society of Anesthesiologist (ASA) physical status I, II, and III were included. Patients excluded were (1) intubated; (2) non–English speaking; (3) identified by the 3D-CAM tool to show evidence of delirium at the preoperative assessment; or (4) diagnosed with dementia or profound aphasia or both.

Assessing Delirium

Many tools have been validated to identify delirium, including the Confusion Assessment Method (CAM),[13] CAM for the ICU (CAM-ICU),[14] and the 3D-CAM.[15] Each of these tools diagnoses delirium based on criteria identified by the Diagnostic and Statistical Manual of Mental Disorders. The CAM has strong validation results, but the lengthy cognitive assessment and requirement of clinician training limits its use in the clinical setting.[15] As a result, the 3D-CAM was created. It is a structured tool that takes a median time of 3 minutes to complete and indicates the presence or absence of delirium.[15] The scale focuses on the four diagnostic features of the CAM.[15] These four key features of delirium are identified using two techniques. Cognitive function is assessed with a series of questions and the patients' speech and behavior are observed to determine the level of consciousness.[15] Patient responses to questions 1 to 7 of the 3D-CAM are used to determine cognitive functioning whereas questions 8 to 10 allow patient-reported delirium symptoms. Questions 11 to 22 are completed by the observer, and preoperative to postoperative status is compared to determine the level of consciousness. Delirium is considered present when a patient exhibits both features 1 and 2, and either feature 3 or 4.[15]

1. Acute onset or fluctuating course of mental status.
2. Inattention.
3. Disorganized thinking.
4. Altered level of consciousness.[15]

The 3D-CAM tool was validated against a reference standard, which is a 15-minute cognitive examination followed by the CAM.[15,16] The 3D-CAM tool has a sensitivity of 95% and a specificity of 94% in diagnosing delirium in hospitalized patients.[15] Permission for its use was obtained[16] and project-specific time points were added to facilitate data collection.

Spinal fusion patients meeting the inclusion criteria were interviewed at a total of five different time points. Preoperatively, the interview consisted of the 3D-CAM tool and verification of their current pain score. After surgery, patients were assessed at four time points with the 3D-CAM tool including (1) arrival to the postanesthesia care unit (PACU), (2) 30 minutes after PACU arrival, (3) 60 minutes after PACU arrival, and (4) 90 minutes after PACU arrival. At each time point, the total pain medication requirement and the pain score were evaluated. To ensure consistency in measurement, a registered nurse served as the single project coordinator and assessed the patients at each time point. The creators of the tool note that 3D-CAM training is required for physicians and nurses before use yet emphasize that it is simple, clear, and succinct to use. A free training manual is available at http://www.hospitalelderlifeprogram.org.[15]

Evidence-Based Innovation

Using the combined results of randomized controlled trials, manufacturer recommendations, American Pain Society recommendations, Lexicomp guidelines, and facility pain service guidelines, the current guideline of initiating an intraoperative ketamine infusion of 4 mcg/kg/min was decreased to 2 mcg/kg/min while maintaining the initial bolus of 0.5 mg/kg.

Implementation Phase

After preimplementation data collection, the baseline incidence (n, %) of delirium was calculated. The data that represented the incidence of delirium associated with anesthetic practices before the ketamine dose change were shared with nurse anesthetists and attending anesthesiologists and residents. These anesthesia providers were also educated on the benefits of low-dose intraoperative ketamine for spinal fusion patients and instructed to use the new ketamine infusion guideline of 2 mcg/kg/min. Multiple educational modalities were instituted including (1) in-person education at the monthly anesthesia departmental meeting, (2) e-mail, and (3) an information sheet attached to the anesthesia cart in each operating room with spine surgeries.

Attempting to promote adoption, an initial 2-week phase followed the educational phase during which anesthesia providers were reminded of the new ketamine guidelines. Time was allotted for and staff were encouraged to ask questions. Reminders were sent through e-mail to the anesthesia providers the night before surgery for scheduled spinal fusion cases. The guideline was attached to each e-mail for easy viewing and a laminated hard copy was attached to the side of the anesthesia gas machines in applicable spine surgery operating rooms. Anesthesia providers were also instructed to relay questions about the guideline to the project coordinator via the e-mail address provided in the daily reminder e-mail. All questions were addressed by the project coordinator or the department chair of neuroanesthesia. After the 2-week initial phase, a

4-week implementation phase started. This action allowed time for the facility to adopt the revised guideline and expose anesthesia providers to the new ketamine dosing regimen before postimplementation data collection.

Data Analysis

Baseline delirium rates were evaluated using descriptive statistics, number (n), and percent (%). *Z*-test for differences in independent proportions was used to compare the incidence of postoperative delirium using the preimplementation data to the postimplementation data as measured by the 3D-CAM scores at the five identified time points: (1) in preoperative holding, (2) arrival to the PACU, (3) 30 minutes after PACU arrival, (4) 60 minutes after PACU arrival, and (5) 90 minutes after PACU arrival. Post hoc Cohen's *d* equivalent values were also calculated and used to estimate effect size and explore clinical significance of the difference in the incidence rates at each time point.

Mann-Whitney *U* tests were conducted to compare minutes to opioid request and the hydromorphone requirement in the PACU because of small sample sizes and lack of normality of the data distribution for at least one group. Post hoc η^2 was derived to explore the clinical significance of continuous outcomes. Two-tailed tests were performed with the level of significance set at .10 for each test to safeguard against type II (false negative) errors associated with small sample sizes of this exploratory pilot study. All data analyses were conducted using IBM Statistical Package for the Social Sciences (SPSS) Software (Version 24, IBM, Armonk, NY).

Results

The preimplementation group (n = 14) received a ketamine infusion of 4 mcg/kg/min, whereas patients in the postimplementation group (n = 16) received an infusion of 2 mcg/kg/min. Both groups received an initial ketamine bolus of 0.5 mg/kg before initiation of the infusion. No statistically significant difference was found between preimplementation and postimplementation groups on any demographic, past medical histories, or surgical time (Table 1). There was an expected decrease in the total amount of ketamine administered (adjusted for body weight) to each patient between the protocol groups (−0.3 mg/kg; 95% confidence interval [CI] −0.6, −0.03; $P = .032$) (Table 2). Providers gave more fentanyl at the beginning of the case in the postimplementation group (−3.6 mcg/kg; 95% CI −4.6, −2.6; $P < .001$); however, there was no difference in the total sufentanil or lidocaine administered between protocol groups.

Incidence of Postoperative Delirium

Table 3 presents the postoperative delirium rate at each time point for both groups. No patients in either the preimplementation or the postimplementation group exhibited delirium at the preoperative assessment. There were three postoperative time points where the difference in the incidence of delirium was statistically different between the protocol groups—on arrival in the PACU the difference was 24.1% (95% CI −5.6%, 49.2%; $P = .099$; Cohen's *d* equivalent 0.98); 60 minutes after arrival in the PACU the difference was 31.3% (95% CI −2.3%, 57.4%; $P = .810$); and 90 minutes after arrival in the PACU the difference was 22.3% (95% CI −5.5%, 48.9%; $P = .100$; Cohen's *d* equivalent 0.98). Although there were large 95% CIs for the estimated differences in the incidence of delirium between the two groups at all three of these time points, the post hoc Cohen's *d* equivalent suggested that there may be a large association with the protocol group.

Opioid Requirement in PACU

The median time to first opioid request in the PACU was 26.5 minutes (Min = 0, Max = 90) in the preimplementation group compared with 17 minutes (Min = 0, Max = 90) in the postimplementation group (Table 4). Although the 9.5-minute median difference in the time to first opioid request was not statistically different between treatment groups ($P = .608$), the post hoc η^2 test suggested that there may be an association with the protocol group ($\eta^2 = 0.01$).

Within the first 90 minutes after PACU arrival, the preimplementation group required 1.2 mg (Min = 0, Max = 12.3) of hydromorphone and the postimplementation group required 1.8 mg (Min = 0, Max = 4.0) of hydromorphone (Table 5). Although the −0.6 mg difference in the total

Table 1. Demographics: Comparing Preimplementation and Postimplementation Group

Demographic	Preimplementation n = 14	Postimplementation n = 16	*P*-value
Age (y) mean (SD)	62 (14.1)	59.4 (9.1)	.544
Gender (Male) n (%)	4 (28.6)	9 (56.3)	.159
Race n (%)			
Caucasian	13 (92.9)	12 (75)	.336
African American	0 (0)	4 (25)	.103
Hispanic	1 (7.1)	0 (0)	.467
BMI category n (%)			.649
Nonobese < 29.9 kg/m^2	7 (50)	11 (68.8)	
Obese > 30 kg/m^2	7 (50)	5 (31.2)	
ASA classification			.999
1-2	5 (35.7)	6 (37.5)	
3-4	9 (64.3)	10 (62.5)	
Premedication n (%)			.642
No premedication	3 (21.4)	2 (12.5)	
Premedication	11 (78.6)	14 (87.5)	
Level of education n (%)			
Pre–High school (HS)/graduated HS	11 (78.6)	10 (62.5)	.440
Associate	3 (21.4)	2 (12.5)	.642
Bachelor's or higher	0 (0)	4 (25.0)	.103
Depression n (%)	57.1 (8)	8 (50)	.730
Anxiety n (%)	3 (21.4)	7 (43.8)	.260
Neurologic disorder n (%)	0 (0)	1 (6.7)	.999
Hypertension n (%)	6 (42.9)	12 (75)	.135
Respiratory disorder n (%)			.587
None	9 (64.3)	10 (62.5)	
Asthma	4 (28.6)	3 (18.8)	
Obstructive sleep apnea	1 (7.1)	3 (18.8)	
Home opioid			.576
0—No home opioids	5 (37.5)	8 (50)	
1—Oxycodone	2 (14.3)	4 (25)	
2—Hydrocodone	1 (7.1)	1 (6.3)	
3—Tramadol	1 (7.1)	2 (12.5)	
4—Tramadol + oxycodone or hydrocodone	1 (7.1)	0 (0)	
5—Oxycodone + MS contin	1 (7.1)	0 (0)	
6—Codeine (tylenol #3)	1 (7.1)	0 (0)	
7—Fentanyl patch + oxycodone	1 (7.1)	0 (0)	
8—Oxycontin + hydrocodone	1 (7.1)	0 (0)	
9—Hydromorphone	0 (0)	1 (6.3)	
Number of levels fused n (%)			.466
1 Level fusion	3 (21.4)	5 (31.3)	
2 Level fusion	3 (21.4)	4 (25)	
3 Level fusion	3 (21.4)	4 (25)	
4-5 Level fusion	1 (7.1)	2 (12.5)	
7-8 Level fusion	1 (7.1)	1 (6.3)	
9-10 Level fusion	1 (7.1)	0 (0)	
11-12 Level fusion	1 (7.1)	0 (0)	
13 Level or greater	1 (7.1)	0 (0)	
Impairment n (%)			.291
No impairment	1 (7.1)	4 (25)	
Hearing impairment	2 (14.3)	0 (0)	

(Continued)

Table 1. Continued

Demographic	Preimplementation n = 14	Postimplementation n = 16	*P*-value
Vision impairment	9 (64.3)	10 (62.5)	
Both vision/hearing	2 (14.3)	2 (12.5)	
Ambulation n (%)			.992
Ambulatory	8 (57.1)	9 (56.3)	
Walker/cane	5 (35.7)	6 (37.5)	
Wheelchair/bedbound	1 (7.1)	1 (6.3)	
Number of previous anesthetics n (%)			.250
Never anesthesia	1 (7.1)	0 (0)	
< 1-5 Anesthetics	6 (42.9)	7 (43.8)	
5-9 Anesthetics	5 (35.7)	9 (56.3)	
>10 Anesthetics	2 (14.3)	0 (0)	
Illicit drug use n (%)	0 (0)	1 (6.3)	.999
Alcohol use n (%)			.999
Low ETOH	14 (100)	15 (93.8)	
Moderate ETOH	0 (0)	1 (6.3)	
Heavy ETOH	0 (0)	0 (0)	
Surgery time (min) mean (SD)	390 (105)	391 (149)	.395

hydromorphone administered was not different between treatment groups (P = .417), the post hoc η^2 test suggested that there may be an association with protocol group ($\eta^2 = 0.02$).

Discussion

Current evidence supports the use of intraoperative ketamine as part of a multimodal perioperative pain management protocol for patients undergoing spine surgery. However, our institution's preimplementation protocol of infusing 4 mcg/kg/min resulted in 92.9% (95% CI 68.5%, 98.7%) of patients experiencing postoperative delirium on arrival in the PACU, and a 28.6% (95% CI 11.7%, 54.7%) incidence of delirium 90 minutes after PACU arrival. We aimed to revise the ketamine protocol, educate the anesthesia department on its use, and attempt to decrease the incidence of postoperative delirium in the PACU without increasing opioid requirements. This exploratory pilot study demonstrated a statistical difference between protocol groups in the incidence of delirium at three time points—on arrival to the PACU, and 60 and 90 minutes after arrival to the PACU. Although there were large 95% CIs for the estimated differences in the incidence of delirium between the two groups at all three of these time points, the post hoc Cohen's *d* equivalent suggested that there may be a large association with the postimplementation group. Furthermore, we did not find any difference in the use of opioids or the

Table 2. Intraoperative Analgesic Administration

Anesthetic	Preimplementation n = 14 Mean (SD)	Postimplementation n = 16 Mean (SD)	Difference (Pre − Post) [95% CI]	*P*-value
Ketamine total dose (mg)	110.9 (46.9)	87.5 (35.9)	−23.4 [−54.4, 7.6]	.134
Ketamine total dose/kg (mg/kg)	1.3 (0.4)	1.0 (0.3)	−0.3 [−6, −0.01]	.03
Lidocaine total dose (mg)	488.6 (376.4)	638.1 (372.7)	197.5 [−83.2, 478.2]	.320
Lidocaine dose/kg (mg/kg)	7.8 (4.2)	9.3 (4.4)	1.5 [−1.8, 4.7]	.398
Sufentanil total dose (mcg)	120.1 (57.9)	97.9 (47.4)	−22.2 [−61.6, 17.2]	.397
Sufentanil dose/kg (mcg/kg)	0.23 (0.05)	0.20 (0.04)	−0.03 [−0.06, 0.00]	.163
Fentanyl total dose (mcg)	419.6 (121.4)	166.7 (70.7)	−252.9 [−326.1, −179.8]	.001
Fentanyl dose/kg (mcg/kg)	5.6 (1.8)	2.0 (0.7)	−3.6 [−4.6, −2.6]	.001

CI, confidence interval; Pre − Post, preimplementation − postimplementation.

Table 3. Delirium at Identified Time Points Using 3D-CAM Tool

Time Point	Preimplementation Delirium Incidence (n = 14) Number (%) [95% CI]	Postimplementation Delirium Incidence (n = 16) Number (%) [95% CI]	Difference (Pre − Post) [95% CI]	*Z*-Test *P*-value	Cohen's *d*-Equivalent*
Preoperative	0 (0%)	0 (0%)	—	—	—
PACU admission	13 (92.9%) [68.5%, 98.7%]	11 (68.8%) [44.4%, 85.8%]	24.1% [−5.6%, 49.2%]	.099	0.98
30 min	8 (57.1%) [32.6%, 78.6%]	7 (43.8%) [23.1%, 66.8%]	13.4% [−20.3%, 43.2%]	.465	0.30
60 min	7 (50%) [26.8%, 73.2%]	3 (18.8%) [6.6%, 43.0%]	31.3% [−2.3%, 57.4%]	.070	0.81
90 min	4 (28.6%) [11.7%, 54.7%]	1 (6.3%) [1.1%, 28.3%]	22.3% [−5.5%, 48.9%]	.100	0.98

CI, confidence interval; 3D-CAM, 3-Minute Diagnostic Interview for Confusion Assessment Method Defined Delirium; PACU, postanesthesia care unit; Pre − Post, preimplementation − postimplementation.

*Cohen's *d* guideline: 0.20 = small effect; 0.50 = medium effect; 0.80 = large effect.

time to the administration of the first postoperative opioid dose between either group. The post hoc η^2 test suggested that there may be an association in these opioid metrics with the protocol group, rather than simply a type II error. This pilot study may spur future studies to investigate whether lower ketamine doses can decrease the incidence of postoperative delirium in the initial 90 minutes postoperatively without decreasing the desired analgesic effect. On the basis of this project model, a future study consisting of two groups with 44 patients in each group would yield an 80% power to determine a difference in delirium between the high- and low-dose intraoperative ketamine doses at the time intervals used in this project (admission to the PACU and 60 and 90 minutes after arrival to the PACU).

One specific group of interest included patients exhibiting delirium at the 90-minute postoperative assessment; however, these patients were not followed further into the postoperative period. Consequently, the duration of their delirium was not determined. In a study of older adults undergoing spine surgery, researchers found that postoperative delirium was more likely to occur on postoperative day 2.[4] Hence, both the timing and frequency of delirium assessment screening are important. Critically ill patients with prolonged postoperative delirium were found to have an increase in mortality, a longer ICU stay, and a longer hospital LOS.[17] In patients who exhibited delirium lasting greater than 24 hours, ICU LOS increased by 3 days, hospital duration increased by 8 days, and hospital mortality increased over 12%, when compared with those without delirium.[17] Lee et al[17] found that patients who exhibited delirium for less than 24 hours, had outcomes that were similar to those who did not exhibit delirium. The data from this study support future studies with 45 to 50 patients per group to determine if intraoperative interventions effect the incidence of delirium in the initial 90 minutes after emergence from anesthesia. It is encouraging that future clinical studies of a reasonable size may be conducted to attempt to modify the clinical trajectory of delirium in spine fusion patients.

For purposes of this project, delirium was determined using the 3D-CAM scale. This scale requires that the patient exhibit specific criteria to diagnose delirium. Emergence from anesthesia follows the cessation of a general anesthetic, involves the transition from unconsciousness to wakefulness, may present as hyperactivity or hypoactivity, and may mimic new onset delirium in the immediate postoperative setting.[17] Although the time required for emergence is variable and multifactorial

Table 4. Time (in Minutes) to First Opioid Request in the Postanesthesia Care Unit

Group	Median Time (min)	Min, Max	Mann-Whitney *U* test *P*-value
Preimplementation (n = 14)	26.5	0, 90	.608
Postimplementation (n = 16)	17.0	0, 90	

Table 5. Hydromorphone Requirement in the Postanesthesia Care Unit

Time Point	Group	n	Median (mg)	Min, Max (mg)	Mann-Whitney *U* test *P*-value
0-30 min	Preimplementation	14	0	0, 1	.608
	Postimplementation	16	0.20	0, 1	
31-60 min	Preimplementation	14	0.52	0, 1.6	.734
	Postimplementation	16	0.60	0, 1.4	
61-90 min	Preimplementation	14	0.24	0, 2.3	.948
	Postimplementation	16	0.37	0, 1.1	
Total	Preimplementation	14	1.17	0, 12.3	.417
	Postimplementation	16	1.75	0, 4	

dependent on factors such as duration of surgical procedure, pharmacokinetics, and pathophysiology, modern advances have increased the speed with which patients emerge from general anesthesia. This indicates that emergence delirium is prolonged beyond times expected for emergence from anesthesia.[18] In attempts to decrease the likelihood of confusion between emergence from anesthesia and emergence delirium, assessments for this project were continued 90 minutes into the postoperative period. No further test was completed to differentiate between emergence and delirium. However, cognitive impairment during emergence from anesthesia has been reported to be predictive of postoperative delirium.[17] At the 90-minute assessment 28.6% of the patients exhibited delirium, which aligns with a review of the literature.

The development of postoperative delirium is likely multifactorial depending on patient vulnerability, predisposing factors, and a precipitating insult.[19] Attempts to attribute one single factor, such as the administration of low-dose ketamine to the development of postoperative delirium, are possible,[20] but patient and surgical variability play a prominent role as well. The patients assessed during this project exhibited multiple risk factors for the development of postoperative delirium. The first step in decreasing delirium is to identify delirium risk factors. These include (1) alcohol and substance abuse; (2) polypharmacy and prescriptions including antidepressants, benzodiazepines, anticholinergics, and atypical antipsychotics; (3) sleep cycle alterations; (4) inadequate pain control; (5) age greater than 65 years; (6) decreased renal clearance; (7) infection or postoperative fever; (8) hearing and vision impairment; (9) poor nutrition and/or functional status; (10) anemia and electrolyte disturbances; and (11) altered first-pass metabolism of medications.[3,21,22] The nature of spine surgery further increased the risk of postoperative delirium because of prolonged surgical duration,[3] increased blood loss,[3] and high pain levels.[4] The analysis revealed that clinicians did administer a larger initial fentanyl dose to the patients in the preimplementation group. There were no differences between the protocol groups in the total sufentanil or lidocaine administered to patients. This may suggest that the higher effect site concentration of ketamine produced by the 4 mcg/kg/min dose compared with the 2 mcg/kg/min dose may not provide a significantly higher component of the intraoperative antinociceptive and hypnotic components of the balanced anesthetic being administered to be detectable. Coupled with data that revealed no difference in the postoperative analgesia metrics, this project suggests that the higher ketamine dose is not essential for the balanced anesthetic administered in our institution for spine fusion surgery.

Limitations

The project was a QI initiative; therefore, it does not have a formal research design. As such, the small sample size limits the interpretation of results, as evidenced by the large CIs in the estimates of the incidence of delirium, and the use of statistical testing and limits consistent with an exploratory pilot study (the 2-tailed α set at 0.10 instead of 0.05, the use of post hoc tests of the effect size rather than just the difference between treatment effects, and so forth). However, these statistical adjustments provide value to this project and inform future investigators of the sample size required for future studies as well as estimates of the effect size of the outcomes of interest when evaluating postoperative delirium as a side effect of intraoperative analgesic administration.

Four of the data collections points were completed in the PACU during a time when emergence from anesthesia is hard to differentiate from delirium.[17] However, cognitive impairment during emergence from anesthesia has been reported to be predictive of postoperative delirium.[17]

An additional limitation of the project was related to interrupted workflow during preoperative and PACU assessments. Creators of the 3D-CAM report that it requires a median completion time of 3 minutes with an interquartile range of 2 to 5 - minutes. The same assessment coordinator was consistent throughout the project and required approximately 5 minutes of uninterrupted time to complete the assessments. During this time, questions were asked about pain scores, data related to pain medication requirements were gathered, and the 3D-CAM was completed. Assessments required coordinated efforts with the postoperative nurses to decrease interruptions in patient care and rest, which could promote patient recovery times. The assessment completed 30 minutes after arrival to the PACU in addition to the standard PACU nursing assessments led to the frequent interruption of patients resting in the PACU. Future considerations should identify optimal assessment strategies to improve identification of postoperative delirium while allowing patient rest. In addition, visual, auditory, or combined impairments may result in altered 3D-CAM scores. It is ideal that patients be provided their respective devices such as a hearing aid or glasses to correct the impairment as soon as safely possible in the postoperative period. Often, devices such as these remain with the patient's family or the preoperative department rather than travel to the operating room with the patient, so this may also have falsely contributed to an assessment of delirium.

Conclusions

As with any change, this QI initiative was dependent on cooperation between multiple providers and perioperative departments. The implementation of a revised ketamine protocol, which included a bolus of 0.5 mg/kg and infusion at 2 mcg/kg/min, may change the incidence of postoperative delirium in the PACU. The data from this study support future studies with 45 to 50 patients per group to determine if intraoperative interventions effect the incidence of delirium in the initial 90 minutes after emergence from anesthesia. Further prospective studies are necessary to obtain ideal ketamine dosages while minimizing negative sequela postoperatively in an already delirium-prone environment. Future studies identifying best practice ketamine administration protocols should also include long-term goals directed at improving quality of life, minimizing chronic pain development, and advancing overall patient satisfaction. In addition, consistent assessment with a validated delirium scale throughout the perioperative period could be included to ensure identification of postoperative delirium not only in the PACU but at various time points extended throughout the hospital LOS to address delirium, if identified. Existing literature supports that postoperative delirium is correlated with increased expense, increased LOS, and increased mortality. Mitigating the presence of postoperative delirium in patients undergoing thoracolumbar fusion has the potential to conserve resources for both patients and facilities.

Acknowledgments

The authors would like to thank Julie Thompson, PhD, the Duke University Hospital perioperative nursing staff, and the anesthesia department for their participation in this project.

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