Pediatric Critical Care Physician-Administered Procedural Sedation Using Propofol: A Report From the Pediatric Sedation Research Consortium Database*

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Objective: Increasing demand for pediatric procedural sedation has resulted in a marked increase in provision of pediatric procedural sedation by pediatric critical care physicians both inside and outside of the ICU. Reported experience of pediatric critical care physicians–administered pediatric procedural sedation is limited. We used the Pediatric Sedation Research Consortium database to evaluate a multicenter experience with propofol by pediatric critical care physicians in all settings.

Setting: Review of national Pediatric Sedation Research Consortium database to identify pediatric procedural sedation provided by pediatric critical care physicians from 2007 to 2012. Demographic and clinical data were collected to describe pediatric procedural sedation selection, location, and delivery. Multivariable logistic regression analysis was performed to identify risk factors associated with pediatric procedural sedation–related adverse events and complications.

Measurements and Main Results: A total of 91,189 pediatric procedural sedation performed by pediatric critical care physicians using propofol were included in the database. Median age was 60.0 months (range, 0–264 months; interquartile range, 34.0–132.0); 81.9% of patients were American Society of Anesthesiologists class I or II. Most sedations were performed in dedicated sedation or radiology units (80.9%). Procedures were successfully completed in 99.9% of patients. A propofol bolus alone was used in 52.8%, and 41.7% received bolus plus continuous infusion. Commonly used adjunctive medications were lidocaine (35.3%), opioids (23.3%), and benzodiazepines (16.4%). Overall adverse event incidence was 5.0% (95% CI, 4.9–5.2%), which included airway obstruction (1.6%), desaturation (1.5%), coughing (1.0%), and emergent airway intervention (0.7%). No deaths occurred; a single cardiac arrest was reported in a 13-month-old child receiving propofol and ketamine, with no untoward neurologic sequelae. Risk factors associated with adverse event included: location of sedation, number of adjunctive medications, upper and lower respiratory diagnosis, prematurity diagnosis, weight, American Society of Anesthesiologists status, and painful procedure.

Conclusions: Pediatric procedural sedation using propofol can be provided by pediatric critical care physicians effectively and with a low incidence of adverse events. (*Pediatr Crit Care Med* 2015; 16:11–20)

Key Words: adverse events; airway obstruction; cardiac arrest; deep sedation; laryngospasm; propofol; risk factors

Pediatric patients undergoing diagnostic studies or invasive procedures benefit from procedural sedation to prevent excessive motion, allay anxiety, and for provision of adequate analgesia. Pediatric procedural sedation (PPS) by nonanesthesiologists outside of the operating room has become quite common, and requests for this service are increasing at rate of approximately 10% per year (1, 2). Because of the rising demand for this service and the relative shortage of anesthesiologists and operating room availability, other pediatric subspecialists such as pediatric critical care (PCC MDs), pediatric emergency medicine physicians, and pediatric hospitalists have stepped in to provide PPS (3–5).

Although PCC MDs are trained and quite experienced in the use of medications for deep sedation and analgesia, providing deep procedural sedation outside of the ICU presents

*See also p. 77.

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potential concerns because of working in less familiar work environments and with a different care team than that in the ICU. Most providers of PPS, including pediatric anesthesiologists, have embraced propofol as the sedative-hypnotic agent of choice where it is sanctioned by hospital policy (1). Among the benefits of propofol are its rapid onset, reliable onset of deep sedation/anesthesia, and short duration of action, which results in rapid recovery, and minimal adverse events (AE) (6, 7)). These features of propofol are particularly valuable in children. When compared with adults, pediatric patients receiving deep sedation are at significantly higher risk for AE and have a lower margin of error for progression to AE (7, 8). PCC MDs may have variable experience with propofol (9, 10).

Most of the studies examining propofol use by PCC MDs have been limited to a single institution's experience, were based on small sample sizes, or have used inconsistent definitions of AE. Because of their relatively small sample sizes, most of these studies are underpowered to report infrequent AEs although all of them conclude that the use of propofol in PPS is associated with a low incidence of AE (1, 9–12). Only one study in the literature (using data from the Pediatric Sedation Research Consortium [PSRC]) has sought to evaluate if major sedation-related complication rates differed between different pediatric subspecialty providers (2). This study found no differences in AE rates between provider subspecialties. However, the study did not examine the impact of location of sedation.

Given the increasing use of propofol for PPS by PCC MDs, it is important to characterize the AE profile associated with its use by PCC MDs accurately. Furthermore, the impact of sedation location on AEs during PPS by PCC MDs using propofol has not been previously studied. We used the PSRC database, the largest multicenter registry of pediatric sedation experience, to evaluate the experience of PCC MDs with delivery of propofol for PPS in all settings. Our objective is to define the patient population managed by PCC MDs better and to describe the nature and frequency of AEs of PPS with propofol. We hypothesized that PCC MDs can effectively deliver elective procedural sedation with propofol in multiple locations inside and outside of the ICU with minimal AEs. In addition, we hypothesize that risk factors such as upper respiratory tract infection, prematurity, age, and American Society of Anesthesiologists (ASA) status will be associated with an AE.

MATERIALS AND METHODS

Study Design and Data Collection

This study was an observational cohort review of a prospectively collected research database. We evaluated the PSRC database to identify all PPS provided by PCC MDs between September 2007 and December 2012. PSRC data collection methodology has been detailed in a report of its first 30,000 sedations in 2006 and another 49,836 sedations in 2009 (3, 12). The PSRC data sharing group comprises 37 self-selected locations, including children's hospitals (both within and separate from general hospitals), and general/community hospitals (Appendix 1). Participating institutions were required to obtain institutional review board approval for data collection, identify a primary investigator, and agree to a standardized methodology for consecutive data collection. The intent of the PSRC database is to describe the nature and rate of events (overall) because they occur in the consortium for children undergoing diagnostic and therapeutic procedures outside the operating room. PSRC data are offered as an observational and descriptive set of information to assist in understanding this area of care because it occurs at member institutions. Definitions for events and AEs are discussed and agreed upon by the member institutions at yearly meetings. All members are asked to complete data audits every 6 months that assure the appropriate number of records has been submitted and that there are no systematic errors in the manner in which data are being completed.

PSRC uses a web-based data collection tool composed of 25 primary screens and a dynamically generated interface for each subsequent question according to previous responses. PSRC database records demographic data, the location and nature of the procedure performed, the use of adjunctive medications, and the presence or absence of several predefined AEs. Informed consent was waived because all data are deidentified. The use of multicenter data for quality and research analysis is approved as part of the PSRC data agreement. This study looked at elective sedations performed by PCC MDs and not sedations performed as a part of the care of critically ill patients in a PICU.

In November 2011, the PSRC changed its online data collection template. As a result, definitions of various adjunctive medications, primary diagnoses, and AEs changed. Only variables available in both the 2007 to 2011 and the 2011 to 2012 cohorts were used in analysis.

Outcome and AE Measures

Successful completion of a procedure was documented as an outcome measure. We assessed the incidence of AE and serious AEs (SAE) as outcome measures. A list of these AEs is provided in Appendix 2. A SAE was defined as any one of the following events: 1) airway obstruction, 2) laryngospasm, 3) emergent airway intervention, 4) unplanned hospital admission or increased level of care, 5) aspiration, 6) emergency anesthesia consult, 7) cardiac arrest, or 8) death. These SAE are readily identifiable in the sedation database. Emergent airway intervention, as defined in the PSRC database, includes tracheal intubation, positive pressure ventilation, or placement of another airway device (oral airway, nasopharyngeal tube, or laryngeal mask airway) because of prolonged apnea or oxygen desaturation. Airway obstruction was defined as lack of air movement in spite of respiratory effort. Laryngospasm was defined as complete or near-complete lack of air movement with respiratory effort and/or stridor, not relieved by chin repositioning or oral/nasal airway. Although multiple AE could occur within a single course of sedation, the AE rate was reported as the number of sedations in which at least one AE occurred out of the total number of sedations. Additionally, patients could have been sedated more than one time and appear multiple times in the dataset. For analysis, multiple

sedations on the same patient were considered independent. Information was only available on pre-, intra-, and immediate post-procedure events and long-term follow-up or any subsequent care related to an AE could not be obtained.

Statistical Methods

Descriptive statistics were calculated using counts and frequencies, medians and ranges, or means and CIs for patient demographics and sedation procedure characteristics. AE and SAE rates were calculated, and 95% CIs for these rates are provided. AE rates were also calculated by location of sedation, and chi-square tests were used to determine whether rates varied by location. To control for multiple testing, a Bonferroni correction was applied and multiple comparisons between locations were considered significant at the 0.008 level. Multiple variable logistic regression was used to identify risk factors associated with an AE. Adjustment for individual center effect was not performed because of the potentially large number of confounders, such as case mix, ASA status, and referral patterns, that make it difficult to compare across centers in the database. Potential risk factors were identified because of their historically known or demonstrated association with the occurrence of an AE and included: location of sedation, primary diagnosis, age, weight, sex, ASA physical status greater than or equal to 3, the number of adjunctive medications in addition to propofol, painful procedure (Appendix 3), nothing by mouth for solids and clear liquids, and mode of propofol (bolus only, infusion only, and bolus plus infusion) administration. Because of the high correlation between age and weight (r = 0.867), only weight was included in the models and was dichotomized as less than 5 or greater than or equal to 5 kg. Weight was dichotomized as less than 5 and greater than or equal to 5 kg, which provides an easier interpretation of the model odds ratios for the clinician. This dichotomization is also similar to what has been done in a previous study (13). All variables were initially included in the model. A modified backward elimination procedure was used, and nonsignificant variables were systematically removed, provided the model fit did not significantly change. Statistical significance was assessed using a significance level of 0.05, unless otherwise noted, and two-sided statistical tests are reported. All statistical analyses were performed using SAS 9.3 (Cary, NC).

RESULTS

Demographics and Sedation Characteristics

Between September 2007 and December 2012, 91,189 procedural sedations performed by PCC MDs using propofol were reported. Demographic and sedation characteristics are provided in **Tables 1** and **2**. The majority of patients were less than 12 years old and over one half (51%) were less than or equal to 60 months. Boys were slightly more prevalent than girls. Most patients (81.9%) were ASA physical status I or II. A small number of patients (1.2%) had a documented NPO time for solids of less than 6 hours prior to sedation. More than 94% of patients received propofol through bolus administration

TABLE 1. Summary of Demographics of Patients Receiving Pediatric Procedural Sedation by Pediatric Critical Care Physicians

Characteristic	n = 91,189
Age (mo), median (25–75%)	60.0 (34.0–132.0)
Weight (kg), median (25–75%)	21.0 (14.0–39.4)
Sex, men (n = 91,180) (%)	50,094 (54.9)
American Society of Anesthesiologists physical status (n = 90,729) (%)	
1	15,080 (16.6)
2	59,237 (65.3)
3	16,177 (17.8)
4	144 (0.2)
≥ 5	91 (0.1)
NPO clear liquids (hr) (n = 89,864) (%)	
< 2	453 (0.5)
≥ 2	89,411 (99.5)
NPO solids (hr) (n = 90,488) (%)	
< 6	1,059 (1.2)
≥ 6	89,429 (98.8)
Primary diagnosis (%)	
Hematology/oncology	27,513 (30.2)
Neurological	24,065 (26.4)
Gastrointestinal	17,231 (18.9)
Infection	4,460 (4.9)
Other	3,860 (4.2)
Renal	2,793 (3.1)
Orthopedics	2,626 (2.9)
Respiratory: lower airway	1,389 (1.5)
Surgical/wound management	1,266 (1.4)
Cardiovascular	1,120 (1.2)
Metabolic/genetic	1,095 (1.2)
Rheumatology	813 (0.9)
S/P transplant	691 (0.8)
S/P trauma	636 (0.7)
Dermatologic	603 (0.7)
Liver disease	585 (0.6)
Craniofacial abnormalities	492 (0.5)
Congenital conditions	475 (0.5)
Burn injury	423 (0.5)
Respiratory: upper airway	399 (0.4)
Immune compromise	195 (0.2)
Prematurity related	88 (0.1)
Dental	68 (0.1)

NPO = nil per os (nothing by mouth), S/P = status post.

TABLE 2. Summary of Pediatric Procedural Sedation Characteristics Performed by Pediatric Critical Care Physicians

Characteristic	*n* = 91,189
Propofol administration (%)	
Bolus only	48,179 (52.8)
Infusion only	4,532 (5.0)
Bolus and infusion	38,062 (41.7)
No administration data	416 (0.5)
Place of sedation (%)	
PICU	3,662 (4.0)
Radiology/sedation unit	73,785 (80.9)
Dental	40 (< 0.05)
Emergency department	143 (0.2)
Specialty clinic/floor	8,576 (9.4)
Cardiac catheterization suite	137 (0.2)
Other	4,846 (5.3)
Painful procedures[a]	44,019 (48.3)
Adjunctive medications (%)	
Lidocaine	32,197 (35.3)
Opioids (morphine/fentanyl)	21,231 (23.3)
Benzodiazepines[b] (midazolam and ativan)	14,930 (16.4)
Anticholinergics (glycopyrrolate and atropine)	7,467 (8.2)
Ketamine	3,804 (4.2)
Chloral hydrate	128 (0.1)
Barbiturates (pentobarbital and methohexital)	109 (0.1)
Etomidate	6 (< 0.01)

[a]Painful procedures are defined in Appendix 3.

[b]Use of benzodiazepines may be underestimated because of changes in the data collection in 2011.

(either bolus alone or bolus and infusion) and 62% of patients received at least one adjunctive medication with propofol. The most frequently used adjunctive medications were lidocaine (35.3%), opioids (23.3%), benzodiazepines (16.4%), and anticholinergics (8.2%). Eighty-one percent of patients were sedated in either a radiology or a sedation unit. The most common primary diagnosis was hematology/oncology (30.2%) followed by neurological (26.4%) and gastrointestinal (18.9%). Patients were sedated for a variety of procedures. The most common procedures were radiology (40.7%) followed by hematology/oncology (24.8%), gastroenterology (19.7%), and surgical (10.2%) (**Fig. 1**). The overwhelming majority of procedures were successfully completed (99.9%); only 118 procedures could not be completed, secondary to the AE.

AE and SAE

Of 91,189 recorded sedations, 4,596 sedations had one or more AE (5.0%; 95% CI, 4.9–5.2%), with 6,801 total AE reported. In 1,342 (1.5%) of the 91,189 sedations, more than one AE was reported. Of the 91,189 sedations, 2,012 had one or more SAE (2.2%; 95% CI, 2.1–2.3%), with 2,345 total SAE reported. In 279 sedations (0.31%), more than one SAE was reported. The most common AEs and a list of all SAEs are provided in **Tables 3** and **4**, respectively. Among the five most common AE, two were considered serious (airway obstruction and emergent airway intervention). All other AEs considered were extremely rare and occurred in less than 0.5% of sedations.

No deaths were reported. Cardiac arrest was reported in only one patient. This patient was a 13-month-old child with history of genetic/metabolic disease, sedated for MRI had a cardiac arrest intraprocedure. She experienced airway obstruction, desaturation, and hypoxemia requiring intubation. She received 30 seconds of chest compressions and was admitted to the PICU after intubation. Within 2 hours, she was extubated and survived without any neurologic or other sequelae.

AE and serious adverse rates varied significantly by location (**Fig. 2**) ($p < 0.001$ for both rates). Although sedations by intensivists in dental suites were rare (< 0.05%), the AE rates were the highest in this location (25.0%), followed by cardiac catheterization suites (13.9%), "other" locations (8.4%), and the PICU (6.7%). Radiology/sedation units were the most common location for sedation (80.9% of the total), and the overall AE rate was 4.7%. Radiology/sedation units had a significantly lower AE rate when compared with the PICU (6.7%; $p = 0.001$), dental suites (25.0%; $p = 0.008$), specialty clinic/floor unit (5.4%; $p = 0.001$), cardiac catheterization suite (13.9%; $p < 0.001$), and other locations (8.4%; $p < 0.001$) but was not significantly different from the emergency department (ED) (4.2%; $p = 0.946$). SAE rates were highest in dental suites (10.0%) followed by cardiac catheterization suites (8.0%) and "other" locations (4.5%). The ED had very few SAE ($n = 2$; 1.4%), followed by radiology/sedation units (2.0%). Similar to the comparison of AE rates among locations, the radiology/sedation location had a significantly lower SAE rate when compared with the PICU ($p < 0.001$), dental suites ($p = 0.008$), specialty clinic/floor units ($p < 0.001$), cardiac catheterization suites ($p < 0.001$), and "other" locations ($p < 0.001$) but was not significantly different from the ED ($p = 1.000$).

Risk Factors for AEs

The final multiple variable logistic model included the variables location of sedation, the use of adjunctive medication with propofol, primary diagnosis of a lower respiratory infection, primary diagnosis of prematurity, primary diagnosis of upper respiratory infection, weight, ASA status, and painful procedure (**Table 5**). NPO status of less than 6 hours prior to sedation was not associated with increased risk of AE. After adjusting for ASA status, diagnosis, weight, and adjunctive medication, location of sedation was still a significant predictor of an AE. Patients with a primary diagnosis of a lower respiratory infection had significantly higher odds of an AE

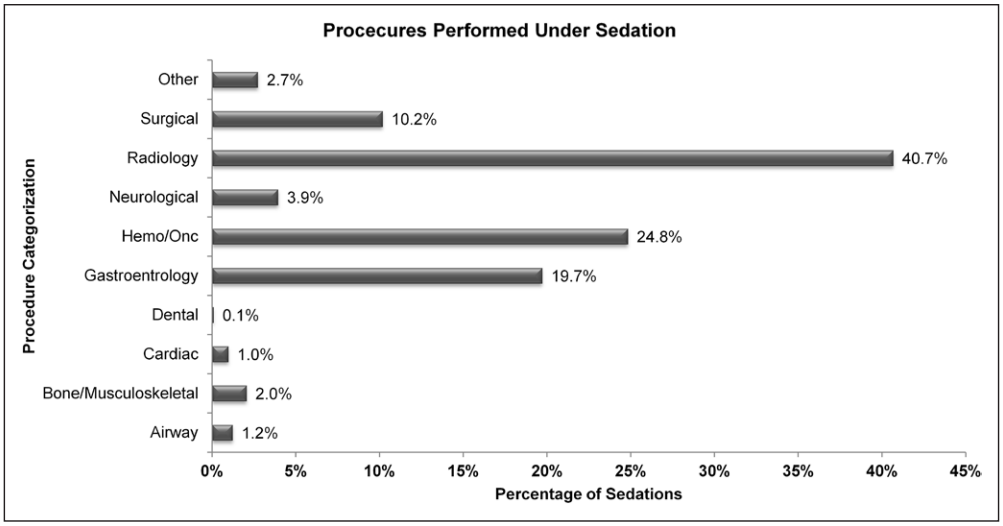

Figure 1. Summary of procedures performed under sedation. Patients can be sedated for more than one procedure so percentages do not total to 100. Airway (bronchoscopy, laryngoscopy, and other); bone/musculoskeletal (botox injection, cast placement/removal, fracture reduction, joint injections/reductions, pin removal, and other); cardiac (cardiac catheter, cardioversion, echocardiogram, electrophysiology study, ablation, pericardiocentesis, transesophageal echocardiogram , and other); dental (dental restoration, tooth extraction, and other); gastroenterology (cecostomy change/placement, colonoscopy, liver biopsy, manometry, percutaneous endoscopic gastrostomy/gastrostomy tube placement/change, pH probe, upper endoscopy, and other); hematology/oncology (bone marrow aspiration/biopsy, lumbar puncture (LP)/intrathecal meds, radiation therapy, other); neurological (brainstem auditory response test, electroencephalography, electromyography, epidural blood patch, LP (diagnostic), magnetoencephalography, somatosensory evoked potentials, and other); radiology (CT, dual energy radiograph absorptiometry, MRI, magnetic resonance angiography, magnetic resonance venography, magnetic resonance spectroscopy, nuclear scan, positron emission tomography, peripheral inserted central catheter placement, transthoracic echocardiogram, ultrasound body, voiding cystourethrogram, venogram/ateriogram, and other); surgical (anal dialatation, arterial line, broviac catheter removal/placement, central line removal/placement, chest tube, circumcision, fine needle aspirate, foreign body removal, incision and drainage abscess, intraoral, laceration repair, peritoneal dialysis catheter placement, PICC line placement, skin biopsy, renal biopsy, suture removal, wound burn care, and other); other (other painful/nonpainful procedure, ophthalmology, exam under sedation, sexual assault exam, and other not classified elsewhere).

when compared with those that did not have a lower respiratory infection (odds ratio, 2.80; 95% CI, 2.39–3.28). Similarly, a diagnosis of an upper respiratory infection was also associated with increased odds of an AE. The odds of having an AE in patients with an ASA status of greater than or equal to 3 were 1.5 times greater than patients with ASA less than 3. A primary diagnosis of prematurity was extremely rare (0.1%) but was associated with increased odds of having an AE (odds ratio, 2.02; 95% CI, 1.05–3.88). For patients undergoing a painful procedure, the odds of an AE were significantly lower than those not undergoing a painful procedure (odds ratio, 0.73; 95% CI, 0.68–0.78).

TABLE 3. Overall Adverse Event Rate and Five Most Common Events

Adverse Event	*n* (%)	95% CI
Overall Adverse Event Rate[a]	4,596 (5.0)	4.90–5.18
Airway obstruction[b]	1,421 (1.56)	1.48–1.64
Desaturation	1,350 (1.48)	1.40–1.56
Coughing	874 (0.96)	0.90–1.02
Emergent Airway Intervention[b]	618 (0.68)	0.63–0.73
Secretions	463 (0.51)	0.46–0.56

[a]Defined as the percentage of sedations where at least one adverse event occurred.

[b]Denotes a serious complication.

DISCUSSION

This study describes experience from the largest cohort to date of PPS by PCC MDs in children undergoing diagnostic and therapeutic procedures outside the operating room using propofol. Results demonstrated efficacy of PPS delivery in multiple settings using propofol by PCC MDs. Our results are consistent with a smaller PSRC cohort study, demonstrating that PPS by trained sedation teams, including PCC MDs, is highly effective with a low rate of SAE (12).

The overall AE incidence in PPS by PCC MDs was 5%, and the SAE rate was 2.2%. In a prior comparative review of specialty providers from the PSRC database from 2004 to 2008, Couloures et al (2) identified a major complication rate of 9.6/10,000 sedates (0.096%) for PCC MDs. Of note, in that large study, there were no differences in AE s among PPS episodes provided by anesthesiologists and emergency medicine physicians. The authors defined major complications as death, cardiac arrest, emergency anesthesia consult, aspiration, and unplanned admission or increase in level of care. When evaluating our more recent database review for the same subset of complications, we found a lower major complication rate of 6/10,000 sedates (0.060%). We elected to define an SAE rate that include the above complications, as well as emergent airway intervention, airway obstruction, and laryngospasm, for an overall SAE rate of 212/10,000 sedates (2.12%). We determined that these additional complications were important to identify as SAE to give the broadest assessment of potential AEs faced by PCC MDs providing sedation. Airway obstruction, the most common complication in this study, can be the initial event in the pathway to pediatric respiratory or cardiac arrest (14, 15). Pediatric patients are more likely to have an acute upper airway obstruction caused by smaller airway caliber and increased compliance of airway cartilage when compared with adults (16). Also, studies have shown that increasing depth of propofol anesthesia in children is associated with upper airway obstruction (17, 18). We also reported laryngospasm because of its association with commonly used drugs, painful procedures, and high likelihood of requiring airway interventions (19). Given the frequency, varying physiologic etiologies in children, and multiple management modalities, identification, and treatment

TABLE 4. Overall Serious Adverse Event Rate and Individual Event Rates of Each Serious Adverse Event

Serious Adverse Event	*n* (%)	95% CI
Overall Serious Adverse Event Rate[a]	2,012 (2.21)	2.11–2.30
Airway obstruction	1,421 (1.56)	1.48–1.64
Emergent airway intervention	618 (0.68)	0.63–0.73
Laryngospasm	242 (0.27)	0.23–0.30
Unplanned hospital admission/increased level of care	46 (0.05)	0.04–0.07
Aspiration	12 (0.01)	0.008–0.02
Emergency anesthesia consultation	5 (0.006)	0.002–0.01
Cardiac arrest	1 (0.001)	0–0.006
Death	0	0–< 0.001

[a]Defined as the percentage of sedations where at least one serious adverse event occurred.

of airway obstruction are the most critical competency for providers of PPS. Simple interventions by PCC-trained MDs, such as patient positioning (jaw thrust and head tilt/chin lift), suctioning, the use of nasopharyngeal or oral airway, or deepening sedation, could help alleviate airway obstruction (20), and intervention by provision of bag-valve-mask ventilation for laryngospasm could contribute to preventing more severe SAE.

There were no deaths in this patient population. The only cardiac arrest described was associated with airway obstruction. This case illustrates the importance of upper airway obstruction, its early recognition, and appropriate management by skilled sedation providers.

The radiology/sedation unit was the most common location of sedation and thus was used as a reference location against which all other locations were compared. Performing PPS in a consistent location with a dedicated sedation team may contribute to low AE or SAE rate as supported by patient safety and healthcare quality literature (3, 4, 21–23). The experience of trained sedation staff in screening of patients who are appropriate for sedation, monitoring sedated patients, having readily available equipment, and managing the patient's airway may explain why such radiology/sedation units had a low incidence of AE.

We found that AE and SAE rates varied significantly by location of sedation. Although sedations in dental suites were rare, both AE and SAE rates were very high in this location. The odds of an AE were almost nine times higher than the odds of an AE in a radiology/sedation unit. This is consistent with findings from other pediatric dental studies. In these studies, it has been speculated that the higher incidence of AE in pediatric dental offices is attributable to lack of adequate monitoring, the need for multiple medications, and the challenge of quickly accessing and managing a patient's airway (secondary to abnormal head and tongue positions, foreign materials such as cotton and rubber dams,

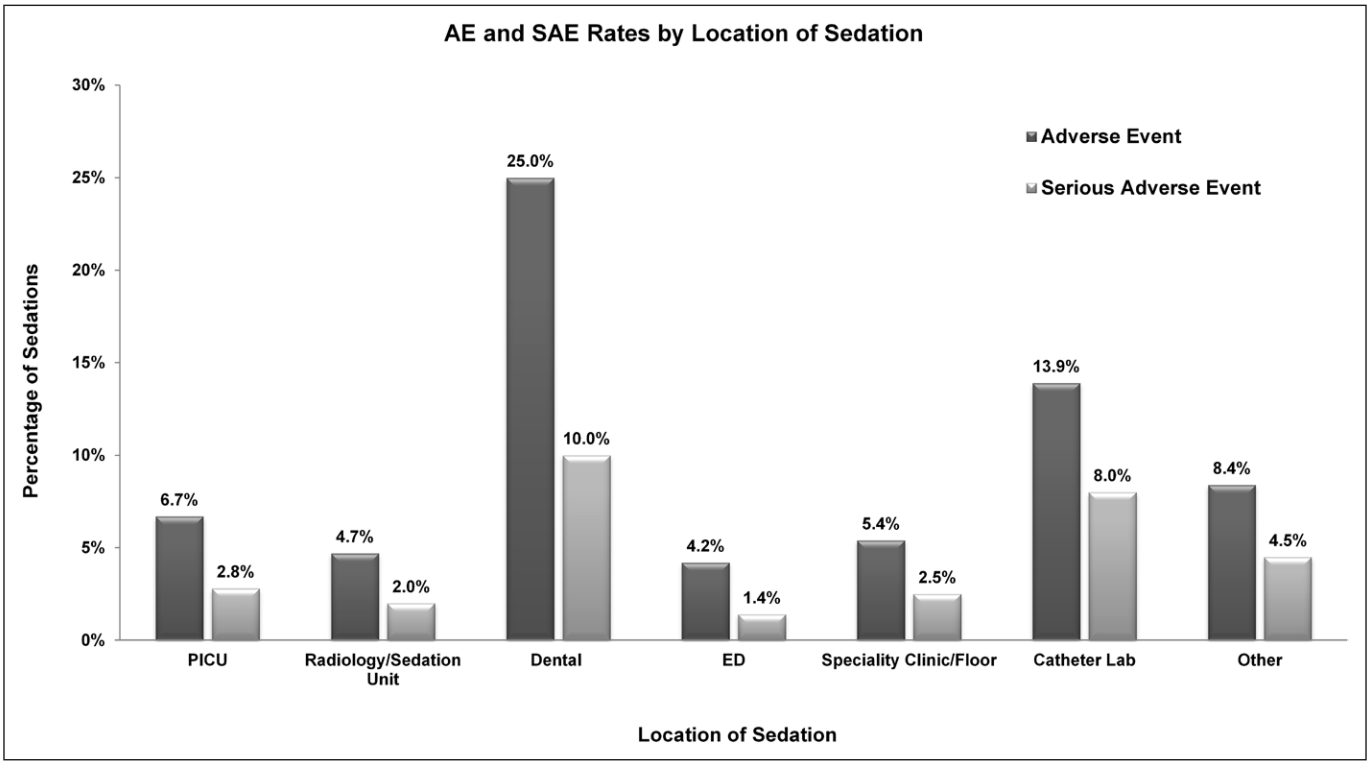

Figure 2. Summary of adverse event (AE) and severe AE (SAE) rates by location of sedation. Rates of AEs and SAEs significantly differed across the locations ($p < 0.001$ for both rates). ED = emergency department.

TABLE 5. Multivariable Logistic Regression: Risk Factors for an Adverse Event

Effect	Level	Odds Ratio	95% CI	*P*
Location of sedation	Dental	8.46	4.10–17.49	< 0.001
	Catheter lab	2.62	1.57–4.36	< 0.001
	Other	1.62	1.45–1.81	< 0.001
	Specialty clinic/floor	1.40	1.26–1.56	< 0.001
	PICU	1.38	1.20–1.58	< 0.001
	Emergency department	1.01	0.44–2.29	0.985
	Radiology/sedation unit (ref)	–	–	–
Adjunctive medication	Propofol + 4 drugs or more	5.83	3.77–9.01	< 0.001
	Propofol + 3 drugs	1.76	1.54–2.01	< 0.001
	Propofol + 2 drugs	1.61	1.48–1.75	< 0.001
	Propofol + 1 drug	1.17	1.09–1.26	< 0.001
	Propofol only (ref)	–	–	–
Primary diagnosis: lower respiratory	Yes	2.80	2.39–3.28	< 0.001
Weight	≤ 5 kg	2.25	1.77–2.87	< 0.001
Primary diagnosis: prematurity	Yes	2.02	1.05–3.88	0.034
Primary diagnosis: upper respiratory	Yes	2.05	1.51–2.78	< 0.001
American Society of Anesthesiologists status	≥ 3	1.46	1.36–1.57	< 0.001
Painful procedure	Yes	0.73	0.68–0.78	< 0.001

Dashes signify radiology unit was used as a reference baseline.

presence of blood, increased secretions, and exogenous water) (7, 24, 25). The odds of developing AE were 2.6 times higher in the cardiac catheterization suite when compared with sedation in a radiology/sedation unit. This is not surprising given the underlying pharmacologic effects of propofol. The cardiopulmonary effects may not be tolerated well in children with congenital heart lesions or depressed cardiac function who are particularly sensitive to changes in preload or afterload. Propofol can alter hemodynamics by decreasing systemic mean arterial pressure and afterload, with increased systemic blood flow. This can result in an increased right to left shunt, and clinically decreased P_{CO_2} and Sp_{O_2} in cyanotic patients (26). Many of the patients with congenital heart disease undergoing cardiac catheterization may have abnormal airway anatomy, pulmonary hypertension, and are at higher risk for develop arrhythmias (27). However, adding the primary diagnosis of cardiovascular condition to the logistic regression model did not significantly improve model fit or was it a significant predictor of an AE. Unfortunately, the PSRC database does not include hemodynamic parameters, such as heart rate and blood pressure, at baseline of regular intervals during sedation. Collecting these parameters in a database would allow for a more convincing analysis and allow separation of hemodynamic from respiratory events.

Risk of AE increased with the addition of adjunctive medications and was almost six times higher in patients receiving four or more drugs in addition to propofol. These results are in line with findings by Coté et al (7), who showed that AEs were frequently associated with drug interactions, particularly when three or more drugs were used. Additional factors demonstrating increased risk of an AE included an ASA status greater than or equal to 3, primary diagnosis of upper or lower respiratory tract disease, prematurity, and small size (weight ≤ 5 kg). These data are consistent with other studies identifying risk factors for AE (9, 12, 28, 29). In this review, 1.2% patients were noncompliant with American Academy of Pediatrics (AAP) sedation NPO guidelines, which call for an NPO time of greater than 6 hours prior to sedation (30). However, our multivariate analysis did not find an association between appropriate NPO status and AEs. A previous study reported that deep sedation of patients undergoing abdominal computed tomography within an hour of by mouth contrast with propofol was not associated with increased AE risk (31). Although patients in the PSRC database with noncompliant NPO status did not demonstrate increased AE risk, we still recommend strict adherence to the AAP sedation NPO guidelines (30).

Patients undergoing painful procedures had a lower risk of developing an AE. This can be potentially explained by the effect of painful procedures to increase patient respiratory activity and alertness caused by the lack of analgesic properties in propofol, thus offsetting the respiratory depression caused by propofol (28). Painful procedures also tend to be shorter when compared with imaging studies, such as MRI scans. For painful procedures, unlike MRI, sedation providers are in constant contact with their patients and are able to anticipate and

initiate management more rapidly, such as repositioning the airway, jaw thrust, providing supplemental oxygen prior to any significant change in vital signs, and administration of additional medications to maintain depth of sedation.

This study has several limitations. The data used in this study come from the PSRC database, which is observational and voluntary in its nature. It is possible that motivation and organization in the 37 member centers reporting would lead to higher performance. As a result, there could be selection bias similar to that present in all sedation/anesthesia studies from single centers reporting their own outcomes. PCC MDs not participating in the PSRC may not have similar results. Additionally, selective data reporting and delay in reporting AE for a particular study period by institutions are possible. However, blinded data submission and internal audits by the PSRC decrease the impact of these effects. Although many PSRC centers likely use similar or identical monitoring approaches (exhaled CO_2 cannulae, etc.) and protocols, the PSRC does not mandate specific standardized or mandated monitoring protocols. Likewise, the PSRC database does not have a method for specific intraprocedure collection of hemodynamic parameters for an entire case. However, hemodynamic parameters are routinely monitored at all centers, and the centers report unexpected change in heart rate (tachycardia, bradycardia) or blood pressure (hypertension or hypotension) that is more than 30% different from baseline. Finally, there are no national benchmarks for definitions of AE (32). We have used the definition for all AE set forth by PSRC, which provides some standardization for the data reporting across the 37 centers (2). Furthermore, we did not take into account AE in relation to the level of sedation. There is a possibility that rate of AEs increase as the depth of sedation increases (30). The determination of the level of sedation requires patient stimulation and is not practical.

CONCLUSIONS

PPS performed using propofol can be performed by PCC MD and can be performed in multiple hospital settings with a very high rate of successful completion and with a low incidence of AE. AE rates are impacted by location of sedation and the use of multiple medications. Although the frequency of transient airway obstruction may be higher than previously thought, airway obstruction can be minimized using a trained provider with proficiency in airway management, appropriate patient and procedure selection, and strict adherence to patient monitoring including the use of end-tidal capnography and pulse oximetry. Immediate access to airway rescue equipment will also help to minimize risk of airway obstruction. To optimize safety, appropriate patient and procedure selection are important. Patients at high risk for complication may be deferred to anesthesia or intubated by the PCC MD prior to the procedure. PCC MDs should ensure that appropriate monitoring, as well as airway rescue equipment, is readily available. Identification and designation of roles to the sedation team members and the use of closed loop communication will help facilitate teamwork and improve efficiency and safety of procedural sedation.

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APPENDIX 1. Participating Centers in the Pediatric Sedation Research Consortium[a]

American Family Children's Hospital, University of WI School of Medicine and Public Health, Madison, WI
Ann & Robert H. Lurie Children's Hospital of Chicago, Chicago, IL
Arizona Children's Center at Maricopa Medical Center, Phoenix, AZ
Avera Mckennan Hospital, Sioux Falls, SD
Blank Children's Hospital - Iowa Methodist Medical Center, Des Moines, IA
Brenner Children's Hospital, Wake Forest Baptist Health, Winston-Salem, NC
Cape Fear Valley Medical Center, Fayetteville, NC
Children's Healthcare of Atlanta at Egleston, Atlanta, GA; Children's Healthcare of Atlanta at Scottish Rite, Atlanta, GA
Children's Hosp of Colorado, Aurora, CO
Children's Hospital at the Medical Center of Central Georgia, Macon, GA
Children's Hospital Medical Center of Akron, Akron, OH
Children's Hospital of the Greenville Hospital System, Greenville, SC
Children's Hospital of The King's Daughters, Norfolk, VA
Children's Hospitals and Clinics of Minnesota, Minneapolis MN
Children's of Alabama, Birmingham, AL
Eastern Maine Medical Center, Bangor, ME
Florida Hospital for Children, Orlando, FL
Gundersen Lutheran, LaCrosse, WI

(*Continued*)

APPENDIX 1. (*Continued*). Participating Centers in the Pediatric Sedation Research Consortium[a]

Helen DeVos Children's Hospital, Grand Rapids MI
Holtz Children's Hospital at the University of Miami/Jackson Memorial Medical Center, Miami, FL
Joe DiMaggio Children's Hospital, Hollywood, FL
Kentucky Children's Hospital, Lexington, KY
Kosair Children's Hospital, University of Louisville, Louisville, KY
Medical University of South Carolina, Charleston, SC
Memorial Children's Hospital, South Bend, South Bend, IN
Memorial University Medical Center The Children's Hospital at Memorial, Savannah, GA
Monroe Carell Jr. Children's Hospital at Vanderbilt, Nashville, TN
Nationwide Children's Hospital, Columbus, OH
Nemours/Alfred I. DuPont Hospital for Children, Wilmington, DE
North Central Baptist Hospital, San Antonio, TX
Palmetto Health Richland Memorial Hospital, Columbia, SC
Rainbow Babies and Children's Hospital, Cleveland, OH
St. Vincent Hospital, Green Bay, WI
The Children's Hospital at Providence, Anchorage, AK
UNC Healthcare, Chapel Hill, NC
UVA Children's Hospital, Charlottesville, VA
WakeMed Children's Hospital, Raleigh, NC

[a]Contributed data to 2007 dataset, 2011 dataset, or both.

APPENDIX 2. Definition of Adverse Events From the Pediatric Sedation Research Consortium Database

Agitation/Delirium
Airway obstruction (no air movement for ≥ 15 s despite respiratory effort)[a]
Allergic reaction
Apnea > 15 s
Aspiration[a]
Cardiac arrest[a]
Coughing
Death[a]
Desaturation: o_2 Sat (< 90) for > 30 s
Emergency anesthesia consultation[a]
Emergent airway intervention[a]
Hypothermia
Inadequate sedation
IV-related complication
Laryngospasm[a]
Secretions excessive enough to require treatment
Stridor
Unexpected change in heart rate or blood pressure > 30%[b]
Unplanned admission to hospital or increase in level of care[a]
Use of reversal agents—unplanned vomiting (nongastrointestinal procedure) Wheezing
Other

[a]Defined as serious adverse event.

[b]Hypertension, hypotension, tachycardia, and bradycardia not present prior to sedation and temporally related to sedation.

APPENDIX 3. Painful Procedures for Which Pediatric Procedural Sedation Was Provided

Bone and Joint/Skeletal
Fracture reduction
Joint injection/aspiration
Joint reduction
Pin removal/placement
Other bone joint/skeletal procedure
Cardiac
Cardiac catheterization
Cardioversion
Electrophysiology study/ablation
Pericardiocentesis
Transesophageal echocardiogram
Other cardiology procedure
Gastroenterology
Cecostomy change/placement
Liver biopsy
Percutaneous endoscopic gastrostomy/gastrostomy tube placement/change
Upper endoscopy
Other gastroenterology procedure
Hematology/oncology
Bone marrow aspiration/biopsy
Lumbar puncture
Ommaya reservoir tap
Radiological
Peripherally inserted central catheter placement
Other
Renal biopsy
Surgical procedure
Dental examination/treatment
Procedure deemed painful