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RELIAS MEDIA

Procedural Sedation and Analgesia in the Emergency Department

Introduction

Procedural sedation and analgesia (PSA), commonly referred to as "conscious sedation" or "procedural sedation," is performed in the emergency department (ED) to alleviate anxiety, decrease pain, and provide amnesia to patients undergoing painful procedures or diagnostic imaging.[1,2] Occasionally, there is a need to achieve deep sedation in the ED, in which a patient is unarousable but will respond purposefully following repeated or painful stimuli. In contrast, general anesthesia is a state of unconsciousness and apnea.[3] The goal of PSA is to achieve moderate sedation, where the patient has depressed consciousness but responds to verbal commands with or without tactile stimulation, or dissociation, where the patient enters a trance-like state. The ideal agent for PSA in the ED provides anxiolysis, analgesia, and amnesia in a rapid and predictable manner, without side effects, and with a quick recovery phase.[4] This paper will review guidelines for performing PSA in the ED, including suggested training, preprocedural assessment, and intraprocedural monitoring. In addition, it will describe some of the commonly used medications for PSA in the ED.

Guidelines for ED PSA

Physicians from multiple specialties routinely perform PSA in various inpatient and outpatient settings, such as the ED, the endoscopy suite, the operating room, and the intensive care unit. As a result, different medical societies have developed unique, specialty-specific guidelines about how PSA should be performed and monitored. A single hospital may have multiple guidelines governing how PSA is performed in different settings. In 2001, the Joint Commission on Accreditation of Health Care Organizations (now known as The Joint Commission) created a policy statement that defined the spectrum of PSA and created qualitative measurements for providers based on many of the standards set forth by the American Society of Anesthesiologists (ASA).[5] However, most ASA guidelines are based on evidence from scheduled, elective PSA encounters, whereas PSA performed in the ED generally is unplanned and emergent. As a result, the American College of Emergency Physicians (ACEP) developed and updated its own PSA guidelines.[6] This practice has been endorsed by the Centers for Medicare and Medicaid Services (CMS), which states: "The ED is a unique environment where patients present on an unscheduled basis with often very complex problems that may require several emergent or urgent interventions to proceed simultaneously to prevent further

EXECUTIVE SUMMARY

- The Centers for Medicare and Medicaid Services (CMS) acknowledges the unique capabilities of emergency physicians to perform procedural sedation and analgesia. CMS permits hospitals to follow specialty guidelines such as those produced by the American College of Emergency Physicians (ACEP) in determining hospital policy.
- ACEP's recent guideline on unscheduled sedation supports the use of ketamine and propofol as appropriate sedation agents when used by qualified emergency physicians.
- Fasting should not be required for sedation. End-tidal CO_2 monitoring does not appear to reduce adverse events.
- Sedative agents should be selected based on the condition of the patient and the type of procedure to be performed.

morbidity and mortality."[7] The authors of this paper agree that hospital-based guidelines on PSA performed in the ED and privileging should focus on whether the emergency provider possesses the knowledge and experience in airway assessment and management, and the rescue skills that might be needed during PSA performed in emergent situations.

PSA Training, Privileging, and Quality Assurance

PSA, advanced airway management (e.g., intubation), vascular access, and resuscitation are considered core competencies in emergency medicine residency training. Emergency medicine residents are expected to have performed at least 15 supervised PSA encounters by graduation.[8] As a result, most emergency medicine-trained physicians are proficient in PSA. For other providers involved in emergent PSA, ACEP's guidelines support what are known as "focused PSA privileges," in which providers demonstrate knowledge and skills pertinent to moderate sedation and do not intend to perform dissociative or deep sedation, although they still possess rescue skills since patients may pass unintentionally to a deeper level of sedation.[6] Often, department medical directors and hospital PSA committees specify "focused PSA privileges" based on an individual evaluation of each provider's competency. PSA curricula, consisting of self-learning and simulation sessions, have been shown to improve provider proficiency in performing PSA, independent of provider profession and clinical experience.[9] Despite wide variability in the credentialing processes, training, and equipment used in different EDs, studies have shown overall low rates of adverse events for PSA in the ED, regardless of the level of training of the provider.[10] Departmental and institutional quality assurance (QA) programs should track adverse events, review documentation, and identify areas for improvement. Although CMS suggests a single physician oversee sedation in a hospital, that physician does not need to be an anesthesiologist.[11]

Personnel for Emergent PSA

ACEP guidelines recommend having at least two trained healthcare providers present during PSA, with at least one who is skilled in vascular access.[6] ACEP, ASA, and The Joint Commission guidelines agree that the provider who oversees the PSA, usually a physician, should be responsible for the patient's global management, including supervision of personnel and identification and management of adverse events.[6,12] In a "single-coverage" ED, this provider also may be expected to perform other brief procedures (e.g., fracture/dislocation reduction), as long as the non-PSA procedure can be halted.[13-15] In ACEP's guidelines, the second provider, usually a nurse or respiratory therapist, primarily is involved with continuous monitoring of the patient and documentation, although this provider can assist with minor, interruptible tasks that do not interfere with monitoring.[6] In practice, often a respiratory therapist and one to two nurses are present and share the duties of monitoring and documentation. In addition, another provider may be available to help with non-PSA procedures. Preprocedural preparation and intraprocedural distraction by child life specialists also have been shown to decrease pain and distress in children undergoing procedures.[16]

Nurse-Administered PSA Medications

Qualified nurses routinely administer sedating medications and paralytics for non-PSA indications, such as intubation, under the supervision of an ordering provider. However, without supporting evidence, many state and nursing regulatory bodies restrict nurses from administering PSA medications in the ED. There is ample evidence that it is safe for nurses to administer PSA medications with the ordering provider present and specifying the medication type and dose.[6,17-19]

Pre-PSA Assessment

When possible, a pre-sedation assessment of a patient should include a focused history and physical exam, including a review of comorbidities, medications, allergies, and prior PSA and anesthesia experiences. Anatomic variants that may put a patient at risk of airway or ventilatory compromise, such as obesity and obstructive airway disease, should be noted. The ASA physical status classification system is used commonly to identify patients at risk for adverse events.[20] (*See Table 1.*) Patients at the extremes of age and with severe systemic disease (i.e., ASA III-VI) have a greater risk of adverse events during PSA.[4,21,22] Of note, the Mallampati score, which is a visual assessment of the oropharynx, has been shown to be unreliably assessed between providers, poorly predicts difficult bag-valve mask ventilation and intubation, and has no impact on clinical outcomes. Therefore, it cannot be recommended as a necessary part of the pre-PSA evaluation.[23-27]

Preprocedural Fasting

Based on the traditional thinking that fasting time contributes to aspiration

risk, many PSA guidelines include requirements for preprocedural fasting. The ASA consensus statement recommends that patients not eat solid foods for six hours or drink clear liquids for two hours prior to PSA or general anesthesia.[28] However, these requirements may not be practical for ED patients. In addition, given that airway reflexes are left intact, there should be no increase in the risk of aspiration.[29] The authors of one study in children undergoing PSA found that although a majority did not meet fasting criteria, there were no aspiration episodes.[30] In addition, there have been no reports in the literature of deaths from aspiration during ED PSA.[3,31] As a result, ACEP guidelines do not consider recent food intake to be a contraindication to PSA, although it may affect the timing and target level of sedation.[1,32,33] In patients with underlying risk factors for aspiration, such as small bowel obstruction, a PSA medication that preserves protective airway reflexes, such as ketamine, is preferred.[34]

Monitoring and Equipment

It is standard practice and consistent with ACEP guidelines to continuously monitor the patient's pulse, oxygen saturation, and respiratory rate during PSA in the ED. Blood pressure typically is measured every five minutes.[6] Clinically significant arrhythmias or hypotensive episodes are extremely rare during PSA in individuals without systemic disease. Supplemental oxygen, suction, and monitoring equipment should be available. In addition, advanced airway equipment, resuscitative medications, and vascular access supplies should be readily accessible.

Carbon Dioxide ($ETCO_2$) Monitoring

End-tidal carbon dioxide ($ETCO_2$) monitoring may be used to detect early signs of respiratory depression.[3,35] (*See Figure 1.*) Supplemental oxygen also can be administered during PSA without affecting $ETCO_2$ readings. However, $ETCO_2$ monitoring during PSA in the ED is expensive and has not been shown to predict episodes of desaturation or reduce the frequency of clinically significant adverse events.[36-40] In addition, transient decreased ventilation or apnea detected with $ETCO_2$ may lead to an unnecessary intervention, such as positive pressure ventilation, which can cause gastric insufflation and an increased risk of aspiration.[41] Therefore, $ETCO_2$ monitoring is not yet considered standard of care in ED PSA.

Monitoring of Responsiveness

Responsiveness may serve as an indirect indicator of patient distress, eventual procedural recall, and ventilatory adequacy.[6] Several sedation/responsiveness scales may be used during PSA, although none have been found to be superior in the evaluation of sedation.[42] Examples include the Observer's Assessment of Alertness/Sedation (OAA/S) Scale, the Ramsay Sedation Scale, and the Richmond Agitation-Sedation Scale.[43,44] In the 2018 update of the ACEP practice guidelines, the authors argue that patient responsiveness to voice or pain at any given moment is functionally irrelevant, as long as the patient has effective ventilation.[6]

Discharge Criteria

Following PSA, the provider should document the PSA course, including drugs and doses administered, adverse events, and rescue interventions. Patients typically are monitored until they return to baseline vital signs, level of consciousness, and neuromuscular activity.[45] Per ACEP guidelines, it is not necessary to demonstrate that a patient is able to tolerate an oral challenge after PSA, since nausea is common and usually self-resolving.[6] Serious adverse effects rarely occur after 30 minutes from final medication administration.[46]

Adverse Events

Adverse events are defined as unexpected and undesirable responses to medications that threaten to cause or cause injury or discomfort to a patient.[11,47] Serious adverse events associated with ED PSA are extremely rare and have a reported incidence of < 1% in most studies.[1,48] Apnea (usually defined as cessation of breathing > 30 seconds), with or without oxygen desaturation, is the most commonly reported adverse event and occurs in approximately 40 per 1,000 sedations.[12,49] However, many apneic episodes resolve with tactile or verbal stimulation of the patient and have no clinical consequences. A review of PSA performed in 3,636 patients in the ED found that only two underwent unplanned intubations. Other adverse events associated with PSA vary according to the medication used and the patient population, and may include laryngospasm, bronchospasm, cardiovascular instability, paradoxical reactions, emergence reactions, and emesis.[48] (*See Table 2.*) Clinically significant hemodynamic changes are rare in patients without serious cardiovascular disease.[6] Delayed side effects, such as restlessness and imbalance, have been reported in children who have received PSA.[50] Adverse events associated with specific PSA medications will be discussed later.

Pediatric PSA

Most of the medications used for PSA in adults that are reviewed in the following sections also are safe in children. About 60% of pediatric PSA performed outside the operating room is related to obtaining radiologic imaging and, therefore, does not require analgesia.[51] In addition, although rare, adverse events are more common in very young children, those with underlying disease, and when multiple sedatives are coadministered.[52]

Commonly Used PSA Medications

The choice of PSA medications should be customized to the patient and procedure being performed. Almost all of the medications used to perform PSA in the ED are considered off-label, despite being safe when administered by providers with proper training.[53] There is inadequate evidence to guide PSA medication selection in pregnancy, although, in most instances, the exposures to medications are brief, the doses are low, and significant adverse pregnancy outcomes are not expected.[6,54] In general, elderly patients require lower initial loading doses of PSA medications than younger adults (commonly half the dose) because of decreased clearance, and medications are titrated to effect. (*See Table 3.*)

Table 1. American Society of Anesthesiologists (ASA) Classification

ASA Classification	Description	Example
ASA I	Normal healthy patient	No medical problems and no/minimal smoking
ASA II	Patient with mild systemic disease	Smoking, pregnancy, obesity, well-controlled diabetes or hypertension, mild lung disease
ASA III	Patient with severe systemic disease that is not incapacitating	Poorly controlled diabetes or hypertension, chronic obstructive pulmonary disease, end-stage renal disease, congestive heart failure with ejection fraction 25-40%, history of transient ischemic attack (TIA) or coronary artery disease
ASA IV	Life-threatening, severe systemic disease	Recent history of myocardial infarction or stroke/ TIA, ongoing cardiac ischemia or severe valve dysfunction, implanted implantable cardioverter-defibrillator, ejection fraction < 25%
ASA V	Moribund patient not expected to survive without procedure	Ruptured abdominal or thoracic aortic aneurysm, intracranial bleed with mass effect, ischemic bowel
ASA VI	Brain dead patient undergoing organ harvesting	

Data from: Doyle DJ, Garmon EH. American Society of Anesthesiologists Classification (ASA Class) In: StatPearls. Treasure Island (FL): StatPearls Publishing; 2019. Available at: https://www.ncbi.nlm.nih.gov/books/NBK441940/. Accessed May 14, 2019.

Propofol

Propofol is a sedative-hypnotic medication with amnestic and sedative properties, but without analgesic properties.[55,56] It is the most commonly used agent for PSA, with rapid onset (less than one minute), short duration (less than 10 minutes), and predictable, dose-dependent potency. Propofol typically is given as an initial intravenous dose of 0.5 to 1 mg/kg over three to five minutes, followed by repeat intravenous boluses of 0.5 mg/kg every three to five minutes as needed for adequate sedation.[57] Studies have shown that the recovery time from propofol is shorter than from midazolam or ketamine, and patients report higher satisfaction with propofol than with benzodiazepines.[58-60] Propofol also has been shown to have antioxidant properties and to decrease the cerebral metabolic rate, which is protective in the setting of brain injury.[61-63] Metabolism of propofol is not affected by liver or kidney disease.[64] Elderly patients typically require lower doses than younger patients because of decreased clearance.[64,65] Propofol can cause dose-related respiratory depression, hypotension, and decreased cardiac output; however, this rarely leads to unplanned intubation, prolonged observation, or complications requiring admission.[65-67] It is often combined with the analgesic fentanyl, which may increase the rates and severity of adverse events. Hypotension associated with propofol may be mitigated when it is combined with ketamine, which tends to increase blood pressure.[68] (*See the section on "ketofol."*) Nausea and vomiting are rare side effects of propofol.

In children, propofol is given as a loading bolus of 1 to 2 mg/kg intravenously, followed by 0.5 to 1 mg/kg boluses until adequate sedation is achieved.[69-71] Children who receive propofol have faster recovery than those who receive midazolam.[58] Desaturations are reported in up to 13% of children, but most resolve spontaneously. Only 3% of children require airway maneuvers and less than 1% require bag-valve mask ventilation.[70-72] Up to 92% of children who receive propofol have transient decreases in systolic blood pressure, typically without clinical signs of decreased perfusion.[72]

Lipid Emulsion. Propofol is prepared in a lipid solvent that induces bradykinin release at the site of injection. As a result, patients who receive propofol via a peripheral vein commonly report pain at the injection site.[73,74] Lidocaine (commonly 1 mL of the 1% concentration) can be given intravenously just prior to or coadministered with propofol to prevent this effect.[75] Short-term infusions of propofol have not been shown to affect serum lipid levels.[64] Allergies to soybeans or eggs are contraindications to propofol use.[76] The lipid emulsion also is a potential medium for bacterial contamination after being opened, punctured, and stored at a room temperature for a prolonged period of time.[77]

Etomidate

Etomidate is an imidazole sedative-hypnotic.[55] It has no analgesic properties and often is coadministered with fentanyl.[78] Given its rapid onset (five to 15 seconds), short duration (five to 10 minutes), and rapid recovery time, it is especially useful for short procedures, such as joint dislocation reduction or obtaining some imaging in children.[79-82] In addition, etomidate maintains hemodynamic stability in the setting of cardiovascular compromise, making it an ideal agent for cardioversion or PSA in hypotensive patients.[83,84] Typically, it is given as an intravenous bolus of 0.1 to 0.2 mg/kg over 30-60 seconds. Repeat boluses of

Figure 1. Monitoring

Table 2. Adverse Events Associated With Specific Procedural Sedation and Analgesia Medications

Medication	Associated Adverse Events
Propofol	Respiratory depression, hypotension, decreased cardiac output
Etomidate	Nausea, vomiting, myoclonus, adrenal suppression
Ketamine	Tachycardia, hypertension, increased cardiac output, hypersalivation, emergence phenomenon, laryngospasm
Midazolam	Hypoventilation , hypoxemia, hypotension, paradoxical stimulatory effect
Fentanyl	Pruritus, nausea, vomiting, respiratory depression

the same dose can be given every three to five minutes as needed.[85] Common adverse events include nausea and vomiting, which may be resistant to antiemetics, and myoclonus, typically characterized by brief tremors.[86,87] In rare cases of severe myoclonus or myoclonus interfering with procedures, treatment consists of midazolam 1 to 2 mg intravenous given every 60 seconds until the myoclonus resolves.[85,88] Respiratory depression leading to oxygen desaturation of < 90% or apnea occurs in only 10% of patients.[87]

Reversal and dose-dependent adrenal suppression have been reported after even a single dose of etomidate.[55,89,90] As a result, the use of a single dose of etomidate for PSA in septic patients has been debated.[91,92] The hypnotic and adrenocortical suppressive effects of etomidate also are prolonged in patients with liver disease.[84]

Ketamine

Ketamine, a synthetic derivative of phencyclidine, induces a dissociation between the thalamocortical and limbic systems of the brain, producing a trance-like state that prevents perception of or response to painful stimuli. It provides amnesia, sedation, and analgesia.[93] Ketamine preserves airway reflexes, spontaneous breathing, and cardiac output, making it a popular choice for PSA in the ED. It has been shown to have a success rate greater than 90% in ED PSA, as defined by high patient satisfaction, adequate analgesia, and lack of procedural recall.[94] An added benefit of ketamine is that it may prevent central sensitization to pain and secondary hyperalgesia to episodes of acute pain.[95-97] When given intravenously, typically as a dose of 1 to 2 mg/kg over 30-60 seconds, ketamine produces clinical effects that occur within one minute and last for approximately 15 minutes.[34,65,97] When given intramuscularly, typically as a dose of 4 to 5 mg/kg, its onset is delayed by five minutes and the effects can be more prolonged and variable.[34] Ketamine also can be given via intranasal, intrarectal, and intrathecal routes.[98] Patients who receive ketamine typically return to mental baseline within 30-60 minutes after administration. The concurrent use of benzodiazepines or barbiturates may decrease recovery agitation but also can prolong the effects of ketamine. Elderly patients have lower clearance and prolonged duration of action of ketamine compared to younger patients.[99]

Ketamine is the most commonly used agent for PSA in children undergoing painful procedures in the ED and receives ACEP's highest level of recommendation based on available evidence.[100] It is not recommended for use in children younger than 3 months of age because of concerns for laryngospasm, airway obstruction, and apnea.[34] Pediatric dosing via the intravenous and intramuscular routes is the same as the adult dosing.

Because of its inhibition of catecholamine reuptake, ketamine can cause sympathomimetic effects, such as tachycardia, hypertension, and increased cardiac output. Caution should be used in patients with known or suspected coronary artery disease.[98] The theory that ketamine increases intracranial pressure has been debunked, and the medication has been shown to be safe in patients with traumatic brain injury.[101] Laryngospasm, thought to be due to a heightened gag reflex, occurs in less than 2% of patients, is usually transient,

Table 3. Some Medications for Procedural Sedation and Analgesia in the Emergency Department[34,57,85,102,116,120,147,148]

Medication	Typical Initial Dosing	Repeat Dosing if Needed	Onset of Action	Duration of Action
Propofol	IV 0.5 mg/kg over 3 to 5 minutes	IV 0.5 mg/kg every 3 to 5 minutes	30 seconds	3 to 10 minutes
Etomidate	IV 0.1 to 0.2 mg/kg push over 30 seconds	IV 0.1 mg/kg every 3 to 5 minutes	< 1 minute	5 to 10 minutes
Ketamine	IV 1 to 2 mg/kg over 30 to 60 seconds	IV 0.5 to 1 mg/kg every 5 to 15 minutes	< 30 seconds	5 to 10 minutes
	IM 4 to 5 mg/kg	IM 2 to 5 mg/kg after 5 to 10 minutes	3 to 4 minutes	12 to 25 minutes
Midazolam	IV 0.5 to 2 mg over 2 minutes	Repeat every 2 to 3 minutes	1 to 3 minutes	30 to 60 minutes
	IN (peds) 0.2 to 0.5 mg/kg given 15 minutes prior to procedure		Within 5 minutes	20 minutes
Fentanyl	IV 0.5 to 1 mcg/kg	Repeat every 2 minutes, maximum total dose of 5 mcg/kg	< 1 minute	30 to 60 minutes

IV = intravenous; IM = intramuscular; IN = intranasal

and often responds to brief bag-valve mask ventilation.[65] The increased secretions associated with ketamine can be pretreated with glycopyrrolate (typically 0.2 mg intravenous) or atropine (typically 0.01 mg/kg intravenous, maximum dose 0.5 mg). Respiratory depression associated with ketamine is rare but has been reported with rapid intravenous administration of ketamine in neonates and in patients with central nervous system injuries.[102] Nausea and vomiting, which develop in approximately 4% of patients who receive ketamine, typically occur once the patient is alert and have not been associated with increased rates of aspiration.[103] These symptoms may be prevented with administration of ondansetron.

"Emergence phenomenon," characterized by agitation or hallucinations during recovery from ketamine, occur in approximately 50% of adults and 10% of children who receive the medication.[104] Administering a small, concurrent dose of midazolam (e.g., 0.05 mg/kg intravenous) decreases the incidence of emergence phenomenon.[105,106] Ketamine should be avoided in patients with schizophrenia since it may exacerbate psychotic symptoms.

Ketofol

Ketofol is the term coined for the combination of ketamine and propofol, which can be mixed in advance or dosed sequentially. The two medications are thought to have complementary and synergistic effects. Propofol may lessen the nausea associated with ketamine.[98] In addition, the sympathomimetic effects of ketamine may reduce the hypotension associated with propofol.[107] Ketofol has been shown to be safer and similarly effective when compared with fentanyl in adults undergoing ED PSA.[108] In a study of pediatric PSA comparing intravenous ketofol (0.5 mg/kg of each component) to intravenous ketamine alone (1 mg/kg), researchers found fewer episodes of nausea and vomiting in the ketofol group, no significant differences in sedation or recovery times, and no clinically significant adverse events in any of the patients.[109] Physicians and nurses have reported higher satisfaction when using ketofol.[110-113]

Midazolam

Midazolam is a benzodiazepine with both amnestic and anxiolytic properties. Given its lack of analgesic properties, it often is combined with an opiate during ED PSA. It is the preferred benzodiazepine for PSA because of its rapid onset (one to three minutes when given intravenously), short duration (30-60 minutes), superior amnestic properties, and low risk of phlebitis.[3,114-116] Typically, it is given as an intravenous bolus of 0.5 to 2 mg over two minutes. Its effects may be prolonged in patients who are obese or elderly or who have renal or kidney disease.[66,116,117] Midazolam also can be given via oral, intramuscular, rectal, intranasal, and intraosseous routes.[65] When given orally, higher doses usually are required, given its high first-pass metabolism, and its effects are less predictable.[116] When given intramuscularly, there is usually slow and unpredictable absorption.[118,119] Intranasal midazolam (commonly given as a 0.2 to 0.5 mg/kg dose), administered via a mucosal atomizer, provides approximately 20 minutes of sedation and is useful for obtaining diagnostic imaging in children or performing minor procedures, such as simple laceration repair.[120-122] It is not licensed for use in children younger than 6 months of age.[69]

Adverse events associated with midazolam include hypoventilation, hypoxemia, and hypotension, which typically are seen with high doses of midazolam. Administration of repeated doses can lead to prolonged sedation due to the accumulation of midazolam and its metabolites.[116,123] When midazolam is combined with opiates, there is a synergic effect on sedation and respiratory depression, which can lead to apnea.[124] Hiccups may occur after administration of midazolam and usually resolve spontaneously.[65] Medications that inhibit the

liver metabolic enzyme p450 oxidase, such as cimetidine, hasten the onset of midazolam and may lead to oversedation.[65] Midazolam crosses the placenta and is category D in pregnancy. A paradoxical, stimulatory effect can occur in some patients who receive midazolam.[125]

Flumazenil, the reversal agent for midazolam and other benzodiazepines, is administered to overly sedated patients who have received benzodiazepines. Typically, it is given as an intravenous dose of 0.2 mg, repeated every one minute for a maximum dose of 3 mg. In children, an intravenous dose of 0.01 mg/kg is given. The use of flumazenil is controversial in ED PSA, since it can precipitate seizures and subsequent airway compromise in patients with a tolerance to benzodiazepines.[126] Flumazenil-precipitated seizures are refractory to benzodiazepines and usually are treated with phenobarbital or propofol.

Fentanyl

Fentanyl is a synthetic opioid with mainly analgesic properties often used in conjunction with other PSA medications. It lacks amnestic or sedative properties. It is the preferred opioid for PSA because of its rapid onset (less than one minute when given intravenously), short duration of action (30-60 minutes), and minimal cardiovascular effects.[127,128] Its high lipid-solubility causes it to be 100 times more potent than morphine in equivalent doses.[129] Because of its unpredictable absorption via other routes, it usually is given intravenously for PSA. It typically is administered as an intravenous dose of 0.5 to 1 mcg/kg every two minutes until desired analgesia is achieved, with a maximum total dose of 5 mcg/kg.[3] Fentanyl is used commonly in combination with midazolam when other short-acting PSA agents are unavailable. In such cases, smaller doses of fentanyl (e.g., 0.5 mcg/kg intravenous) should be given over longer intervals to minimize the synergistic effects of the medications and subsequent oversedation.

Fentanyl is eliminated primarily by the liver and should be used with caution in patients with liver disease. Infants have a slower metabolism of fentanyl and should receive approximately one-third the normal dose.[65] Common adverse events associated with fentanyl include pruritus, nausea, and vomiting. Fentanyl also decreases responsiveness to the stimulatory effects of carbon dioxide, leading to a dose-dependent depression in ventilation.[65] High doses have been reported to cause chest wall and glottic rigidity, leading to difficulty with ventilation, although this has not been reported during ED PSA.[130]

Naloxone acts as an antagonist at opioid receptors and is the reversal agent for fentanyl and other opioids. It is administered as a 0.02 to 0.20 mg intravenous dose, given every two to three minutes until adequate ventilation is achieved while maintaining pain control.[131] In children, a 0.001 to 0.005 mg/kg intravenous dose is administered.[132]

Other PSA Medications

Dexmedetomidine

Dexmedetomidine is a highly selective alpha2-receptor agonist with sedative, anxiolytic, and analgesic properties that has been used for deep sedation. It is a relatively novel medication for ED PSA. It has a rapid onset of action (10-14 minutes), quick recovery time, and high success rate in PSA.[69,133,134] Dexmedetomidine should be used with caution in patients with hemodynamic instability. It also has the ability to potentiate opiates and other sedating medications. Dexmedetomidine has been shown to be effective in pediatric PSA to obtain radiologic imaging and in patients undergoing dental procedures.[135-138] In adults, it typically is given as a 1 mcg/kg loading dose over 10 minutes, followed by a maintenance infusion of 0.6 mcg/kg per hour.[139] In children, it typically is given as 0.5 to 3 mcg/kg intravenous boluses, followed by a maintenance infusion of 0.5 to 2 mcg/kg/hour.[129,135,137,140] Dexmedetomidine also can be given by the intranasal route.[141] The adverse effects of dexmedetomidine (e.g., bradycardia, hypotension) counteract the adverse effects of ketamine (e.g., tachycardia, hypertension), making the combination of the two agents a potentially useful regimen for ED PSA.[142] Dexmedetomidine is eliminated mainly by the liver, and dosing should be reduced in patients with liver disease.[139]

Barbiturates

Methohexital, a barbiturate with a rapid onset of action and duration of less than 10 minutes, has been used for ED PSA for short procedures, such as reductions and cardioversion. It produces a state of unconsciousness but does not provide analgesia. It directly depresses myocardial and respiratory ventilatory centers, which can cause hypotension and apnea, limiting its use in certain populations.[65] Pentobarbital, another barbiturate with a rapid onset of action that can be given via oral, intramuscular, or intravenous routes, has been used to obtain pediatric diagnostic imaging. However, this drug has a long recovery time, limiting its use in the ED.[143-145]

Chloral Hydrate

Chloral hydrate, a sedative-hypnotic, can be given orally or rectally, which makes it appealing for use in children. However, its onset of action can be delayed up to 60 minutes and its effects can last for hours, making it less useful for PSA performed in the ED.[65,143] In addition, a high incidence of adverse events (notably vomiting) and a high failure rate limit its use.[144,146]

Inhaled Agents

Nitrous oxide, an inhaled gas with ultrashort-acting (three to five minutes) sedative, anxiolytic, and analgesic properties, has been used in the past for PSA in the ED. However, its risks of malignant hyperthermia and hypotension, its potential for misuse, and its equipment requirements (e.g., a well-ventilated room with a scavenger system) limit its use.[3]

Conclusion

PSA is a core competency of emergency medicine. Guidelines for performing PSA in the ED vary by institution, but usually are set by hospital-based committees and are based on standards set by medical societies, such as ACEP. Preprocedural fasting is no longer considered to be a requisite in performing PSA in the ED. $ETCO_2$ monitoring has not been shown to reduce rates of adverse events and is not considered standard of care.

There is no single ideal drug for PSA, and emergency providers should understand which medications are best suited for certain patients undergoing certain procedures, as well at the adverse events associated with each medication. In a healthy patient without comorbidities, propofol often is preferred, given its rapid onset and quick recovery. For short procedures and in patients with cardiovascular instability, etomidate is ideal. Ketamine is useful in patients with cardiovascular compromise, given its catecholaminergic effects and limited effects on respiratory drive, and is highly effective in children. Intranasal midazolam may be useful in pediatric procedures in which minimal sedation is required and intravenous access is unnecessary, such as diagnostic imaging. Newer agents, such as dexmedetomidine, may be used more commonly for PSA in the future. Serious adverse events, although extremely rare, should be anticipated in all episodes of PSA. Emergency providers who are trained in airway management, vascular access, and resuscitation are uniquely qualified to address such events and to apply rescue maneuvers.

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CME/CE Questions

1. Which of the following is true regarding ED procedural sedation and analgesia (PSA)?
   a. The Mallampati score accurately identifies patients at risk of adverse events.
   b. Patients with American Society of Anesthesiologists (ASA) scores of III and higher are at greater risk of adverse events.
   c. Patients must be fasting for six hours prior.
   d. End-tidal carbon dioxide monitoring decreases the frequency of clinically significant adverse events.
2. Which of the following is true?
   a. Apnea is the most commonly reported adverse event that occurs during PSA in the ED.
   b. Most apneic episodes with oxygen desaturations that occur during PSA require intubation to resolve.
   c. Supplemental oxygen delivery can cause false "normal" end-tidal carbon dioxide monitor tracings in patients who are experiencing hypoxia.
   d. ED PSA requires a minimum of two physicians.
3. Which of the following is true regarding propofol?
   a. It has analgesic properties.
   b. It induces a dissociation between the thalamocortical and limbic systems of the brain.
   c. It has a shorter recovery time than midazolam or ketamine.
   d. It should not be combined with ketamine because of hypotension.
4. Which sedating medication is most commonly associated with myoclonus?
   a. Propofol
   b. Etomidate
   c. Ketamine
   d. Midazolam
5. Which of the following is true regarding ketamine?
   a. It is contraindicated in children.
   b. It provides amnesia, sedation, and analgesia.
   c. It is unsafe in patients with traumatic brain injuries.
   d. Vomiting, a common adverse event associated with ketamine, has been associated with an increased risk of aspiration.
6. An 80-year-old man undergoes PSA for reduction of a dislocated hip. As he recovers from the PSA, he starts to hallucinate and becomes combative. Which of the following medications did he most likely receive?
   a. Propofol
   b. Etomidate
   c. Ketamine
   d. Midazolam
7. Which of the following is true regarding ED PSA?
   a. Only an anesthesiologist can oversee hospital sedation.
   b. CMS permits specialty guidelines, such as those produced by the American College of Emergency Physicians to determine hospital policies.
   c. CMS and The Joint Commission require that all emergency physicians who perform PSA must have current advanced cardiovascular life support and basic life support certification.
   d. American College of Emergency Physicians PSA guidelines require that two physicians be present for all PSA procedures.

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EMERGENCY MEDICINE REPORTS

Procedural Sedation and Analgesia in the Emergency Department

American Society of Anesthesiologists (ASA) Classification

ASA Classification	Description	Example
ASA I	Normal healthy patient	No medical problems and no/minimal smoking
ASA II	Patient with mild systemic disease	Smoking, pregnancy, obesity, well-controlled diabetes or hypertension, mild lung disease
ASA III	Patient with severe systemic disease that is not incapacitating	Poorly controlled diabetes or hypertension, chronic obstructive pulmonary disease, end-stage renal disease, congestive heart failure with ejection fraction 25-40%, history of transient ischemic attack (TIA) or coronary artery disease
ASA IV	Life-threatening, severe systemic disease	Recent history of myocardial infarction or stroke/ TIA, ongoing cardiac ischemia or severe valve dysfunction, implanted implantable cardioverter-defibrillator, ejection fraction < 25%
ASA V	Moribund patient not expected to survive without procedure	Ruptured abdominal or thoracic aortic aneurysm, intracranial bleed with mass effect, ischemic bowel
ASA VI	Brain dead patient undergoing organ harvesting	

Data from: Doyle DJ, Garmon EH. American Society of Anesthesiologists Classification (ASA Class) In: StatPearls. Treasure Island (FL): StatPearls Publishing; 2019. Available at: https://www.ncbi.nlm.nih.gov/books/NBK441940/. Accessed May 14, 2019.

Some Medications for Procedural Sedation and Analgesia in the Emergency Department[34,57,85,102,116,120,147,148]

Medication	Typical Initial Dosing	Repeat Dosing if Needed	Onset of Action	Duration of Action
Propofol	IV 0.5 mg/kg over 3 to 5 minutes	IV 0.5 mg/kg every 3 to 5 minutes	30 seconds	3 to 10 minutes
Etomidate	IV 0.1 to 0.2 mg/kg push over 30 seconds	IV 0.1 mg/kg every 3 to 5 minutes	< 1 minute	5 to 10 minutes
Ketamine	IV 1 to 2 mg/kg over 30 to 60 seconds	IV 0.5 to 1 mg/kg every 5 to 15 minutes	< 30 seconds	5 to 10 minutes
	IM 4 to 5 mg/kg	IM 2 to 5 mg/kg after 5 to 10 minutes	3 to 4 minutes	12 to 25 minutes
Midazolam	IV 0.5 to 2 mg over 2 minutes	Repeat every 2 to 3 minutes	1 to 3 minutes	30 to 60 minutes
	IN (peds) 0.2 to 0.5 mg/kg given 15 minutes prior to procedure		Within 5 minutes	20 minutes
Fentanyl	IV 0.5 to 1 mcg/kg	Repeat every 2 minutes, maximum total dose of 5 mcg/kg	< 1 minute	30 to 60 minutes

IV = intravenous; IM = intramuscular; IN = intranasal

Adverse Events Associated With Specific Procedural Sedation and Analgesia Medications

Medication	Associated Adverse Events
Propofol	Respiratory depression, hypotension, decreased cardiac output
Etomidate	Nausea, vomiting, myoclonus, adrenal suppression
Ketamine	Tachycardia, hypertension, increased cardiac output, hypersalivation, emergence phenomenon, laryngospasm
Midazolam	Hypoventilation , hypoxemia, hypotension, paradoxical stimulatory effect
Fentanyl	Pruritus, nausea, vomiting, respiratory depression

Supplement to *Emergency Medicine Reports*, June 1, 2019: "Procedural Sedation and Analgesia in the Emergency Department." Authors: Caleb P. Canders, MD, Department of Emergency Medicine, UCLA Ronald Reagan Medical Center, Los Angeles; Gregory E. Tong, MD, Department of Emergency Medicine, UCLA Ronald Reagan Medical Center, Los Angeles; and Nadine El Fawal, University of California at Los Angeles.