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Emergency Medicine Practice
Evidence-Based Education • Practical Application

CLINICAL CHALLENGES:

- **How should you assess** individual patients' risks for procedural sedation and analgesia (PSA)?
- **What are the available agents for PSA** and how should you choose the optimal ones for your patient?
- **What is the best evidence** on monitoring modalities for PSA?

Procedural Sedation and Analgesia in the Emergency Department

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Prior to beginning this activity, see "CME Information" on page 22.

Abstract

Procedural sedation is a common procedure performed in the emergency department and is a fundamental skill for emergency clinicians. With a wide variety of procedures and patient populations, procedural sedation can be systematically tailored to individual patients' needs, in order to optimize safety and efficacy. This evidence-based review distinguishes the various levels of sedation, provides insight on which patients are appropriate for procedural sedation, lists adjuncts that should be used, and reviews considerations for special populations. The differences between the most frequently utilized medications are presented, as well as a discussion of documentation requirements and discharge criteria.

EB MEDICINE

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Case Presentations

CASE 1

A 30-year-old man with no past medical history presents to the ED after falling off a ladder, landing on his right shoulder…

- You perform a 3-view shoulder x-ray and find that his right shoulder is anteriorly dislocated.
- The patient states that he had eaten lunch just prior to this event. The patient is in pain and very resistant to any manipulation.
- You know that procedural sedation will be needed, but you wonder if he is eligible since he just ate . . .

CASE 2

An 80-year-old man with a past medical history of congestive heart failure, hypertension, and diabetes presents to the ED with chest pain…

- His initial ECG demonstrates ventricular tachycardia. He has lower extremity edema with bibasilar rales on exam. He is hypotensive, with a blood pressure of 85/52 mm Hg.
- You make the decision that cardioversion with procedural sedation is indicated, but you wonder what would be the best drug(s) to use, given his comorbidities, and whether his ASA physical status class impacts your decision . . .

CASE 3

A 56-year-old obese woman with a history of alcohol abuse, obstructive sleep apnea, and diabetes presents with multiple deep lacerations…

- She states that she was intoxicated and trying to jump over a wire fence when her leg got caught on the edge and she fell backwards, suffering large lacerations on her right leg as well as her face.
- Both wounds appear to be contaminated. She is hysterical and unable to cooperate with your attempts to irrigate and repair her wounds. She asks for medication to help reduce her pain and anxiety, so you decide to perform procedural sedation.
- Given her comorbidities and presentation, what agent(s) would be safest to use in this patient? What adjuncts would be best for these procedures? What are some expected complications and how can you best prepare for them?

Introduction

Procedural sedation and analgesia (PSA) is a commonly used technique to reduce the pain and anxiety associated with medical procedures performed in the emergency department (ED). By improving the timeliness and success of therapeutic or diagnostic procedures, PSA improves the quality of patient care and satisfaction. PSA is used for painful procedures such as fracture or joint reduction, incision and drainage, tube thoracostomy, cardioversion, lumbar puncture, and complex wound repair, as well as for facilitating imaging studies in uncooperative or young patients. By utilizing sedative, dissociative, and/or analgesic agents in a combined and controlled manner, clinicians can perform urgent or emergent interventions without putting the patient at significant risk for discomfort or side effects.[1]

This issue of *Emergency Medicine Practice* reviews the various selection criteria, agents, and procedures for performing PSA in the ED.

Overview of Sedation Levels

The goal of procedural sedation is to suppress a patient's level of consciousness to facilitate the success of an intervention, in addition to ensuring the patient does not have recollection of the unpleasant event. The depth of sedation should be tailored to the procedure being performed, the needs of the patient, and their risk tolerance level.

Levels of sedation should be viewed as a continuum that begins with mild sedation and culminates in general anesthesia, though the transition from one level of sedation to the next can be difficult to predict and varies from patient to patient. The sedation continuum is not medication-specific, and levels from minimal sedation to general anesthesia can be achieved with all PSA agents (except ketamine). The intent of the sedation, not the agent, helps determine the level of sedation. The levels of sedation include:[2-4]

- **Minimal sedation:** The patient maintains a near-normal level of alertness and responds normally to verbal commands, but may have impaired coordination and cognitive function. Ventilatory and cardiovascular functions are unaffected.
- **Moderate sedation:** The patient has a depressed level of consciousness and responds purposefully to verbal commands, with or without light tactile stimulation. They may exhibit slurred speech and ptosis. The patient's airway remains patent without intervention, ventilation is spontaneous, and cardiovascular function is typically maintained near baseline. Patients are commonly amnesic to the event.

- **Deep sedation:** The patient has a depressed level of consciousness in which they cannot be easily aroused, but they respond purposefully after repeated or painful stimulation. Their independent ventilatory function may be impaired, and they may require assistance in maintaining a patent airway. Cardiovascular function is usually maintained.
- **General anesthesia:** The patient is unresponsive to all stimuli and has absent airway protective reflexes. Spontaneous ventilation is often impaired. Patients often require assistance in maintaining a patent airway, and invasive positive-pressure ventilation is usually required due to depressed spontaneous ventilation. Cardiovascular function may be impaired.

Critical Appraisal of the Literature

A literature search was performed using Medline Epub, MEDLINE® in Process, Embase®, and Cochrane Central Register of Controlled Trials (CENTRAL) from 1997 to present, using the search terms *conscious sedation, deep sedation, moderate sedation, procedural sedation,* and *dissociative sedation*. The search was limited to published English-language articles describing procedural sedation performed exclusively in the ED and included systematic reviews, meta-analyses, multicenter studies, randomized controlled trials, and observational studies. Case series and reports were excluded, except in the setting of exceptionally scarce evidence. Articles describing PSA performed in alternative settings such as the endoscopy suite, dental office, etc were excluded. Using this approach, 2675 abstracts were screened, and 93 articles were included in this review.

The most updated guidelines on PSA from the American College of Emergency Physicians (ACEP),[4] the American Society of Anesthesiologists (ASA),[5] and the American Academy of Pediatrics (AAP)[6] were assessed and incorporated into this review. Various definitions for "adverse outcomes" exist in several of the studies, but event reporting is becoming steadily more homogeneous with the adoption of standardized reporting criteria such as the Canadian consensus-based recommendations for pediatric patients, also known as the *Quebec guidelines*.[7]

Prehospital Care

There is a paucity of literature describing procedural sedation in the prehospital setting. One case series published in 2011 implemented an etomidate protocol for prehospital transport.[8] Seventeen patients who were involved in motor vehicle crashes or had isolated fractures requiring splinting were given 0.1 mg/kg intravenous (IV) etomidate and were monitored for sedation; there were no reported adverse outcomes. Specific data on pain response were not reported.[8] Another case series published in 2015 reviewed 212 cases of ketamine use in prehospital transport.[9] There was 1 episode of hypotension, 1 episode of vomiting, and 6 patients experienced emergence phenomena. However, only 27.8% of cases were documented as having full monitoring performed (capnography, heart rate, blood pressure, and oxygen saturation).[9] No consensus recommendations can be provided at this time regarding PSA in the prehospital setting.

Emergency Department Evaluation

Patient Assessment

To date, no outcome-based studies have demonstrated clear benefit from patient evaluation beyond vital signs, mental status, airway patency, and cardiopulmonary assessment prior to sedation.[5] Despite this, consensus guidelines suggest that there is an increased risk for adverse events in patients who are at the extremes of age; have difficult neck, pharyngeal, or facial anatomy; and who have significant underlying diseases. The ASA Physical Status Classification System has been used for more than 60 years to classify a patient's physical status based on pre-anesthesia comorbidities.[10] It specifies classes ranging from class I (patient is normal and healthy) to class VI (patient is declared brain-dead). An online version of the classification system is available at: https://www.asahq.org/standards-and-guidelines/asa-physical-status-classification-system

A focused history and physical examination should be performed and documented prior to the procedural sedation. The patient's previous experiences with sedation or general anesthesia, medication allergies, current drug and alcohol use, medications, and any underlying medical conditions should be reviewed and documented as well. Patient attributes and medical conditions such as extremes of age, ASA class ≥III (with class III as "patient with severe systemic disease" and class IV as "patient with severe systemic disease that is a constant threat to life"[10]), obstructive sleep apnea, routine use of respiratory depressants, and conditions that would augment drug metabolism, should play a part in the decision to perform sedation.[6] Any anatomic or physiologic variants that would make ventilation difficult or put the patient at risk for airway compromise, such as macroglossia, micrognathia, short neck, history of cervical fusion, obesity, facial hair, facial and intraoral trauma, or a history of obstructive sleep apnea should be identified.

The Mallampati score, which is a graded visual assessment of the pharynx and tonsils, is insensitive for identifying difficult laryngoscopy, difficult intubations, and difficult bag-valve mask ventilation. In addition, a score is difficult to obtain in younger children.

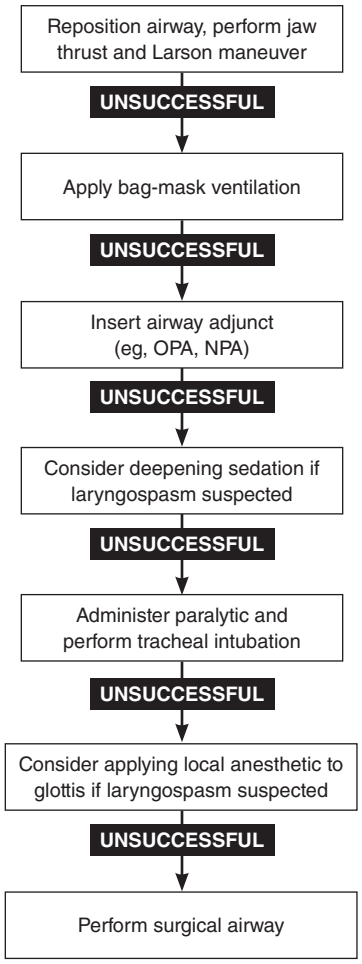
The Mallampati score lacks accuracy, reliability, and feasibility for supplementing standard airway management or procedural sedation in the ED.[11]

Prior to performing the procedure, the depth of sedation required should be determined. Current evidence suggests that increasing levels of sedation results in increasing complication rates. Sacchetti et al reported that cases involving moderate, deep, and (aberrantly involved) general anesthesia had complication rates of 2.6%, 6.3%, and 40%, respectively.[12] The complications for both moderate and deep procedural sedation were related largely to hypoxia that resolved with oxygen administration, bag-valve mask ventilation, or reversal agents. **(See Figure 1.)** Most importantly, all of these complications were able to be managed by the emergency physician and none required any change in the patient's disposition.

In the event of laryngospasm, performing laryngospasm notch pressure (Larson maneuver) may rapidly reverse the condition. To perform the maneuver, apply pressure with the fingertips to the area behind the mastoid process, the ramus of the mandible, and the base of the skull while performing a jaw thrust. **(See Figure 2.)**

A discussion of the risks, benefits, alternative treatments, and potential side effects of sedation should take place with the patient prior to the procedure. Written informed consent for both the procedure and the procedural sedation should be obtained and documented. Airway equipment including a bag-valve mask, oropharyngeal and nasopharyngeal airway devices, and intubation supplies should be readily available at bedside. Additionally, cardiopulmonary monitoring and capnography should be used to monitor the patient throughout the procedure. A code cart/defibrillator should also be available at bedside. (**See Table 1, page 5** for a preprocedural checklist example.) There is no literature to support the need for routine diagnostic testing unless the patient's presenting condition requires it.

Figure 1. Algorithm for Airway Rescue



Abbreviations: OPA, oropharyngeal airway; NPA, nasopharyngeal airway.

Procedural Technique

The Two-Physician Model Versus the One-Physician Model for Procedure Personnel

Current literature does not provide clear evidence for the number and type of personnel necessary to provide safe procedural sedation. There are several observational studies that describe variable levels of personnel at the bedside, with none demonstrating a superior model. For instance, in an observational study of 457 patients requiring sedation for orthopedic reductions, there was no difference in adverse events requiring intervention between cases that had

Figure 2. Laryngospasm Notch Pressure (Larson Maneuver)

Image courtesy of Joshua Kern, MD.

a 1-physician + 1-nurse model versus a 2-physician + 1-nurse model.[13] Similarly, an observational study of 381 procedural sedations found no difference in adverse events or interventions in a 1-physician versus 2-physician model.[14] Additionally, an observational study of 1028 patients performed in community EDs demonstrated no differences in the occurrence of complications when the ED physician performed both the sedation and procedure.[12] Notably, these studies are vulnerable to significant bias, given that staff were able to elect the number of providers to be present. That being said, the ACEP and AAP guidelines for unscheduled sedation currently stipulate that 2 trained healthcare practitioners should be at bedside: the sedation provider who takes responsibility for oversight of the procedural sedation encounter and a sedation monitor (commonly a registered nurse or respiratory therapist) whose primary duty is continuous patient monitoring and documentation.[4,6,15,16]

Table 1. Preprocedural Checklist for Procedural Sedation

- **Personnel**
  - Provider performing the procedure
  - Individual trained in ACLS/PALS (eg, nurse) primarily responsible for patient monitoring
- **Monitoring**
  - Electrocardiogram monitor
  - Blood pressure monitor
  - Pulse oximetry
  - Capnography
- **Sedative/analgesic agent(s)**
- **Documentation**
  - Prior to the procedure
    - Time out: Patient name, date of birth, medical record number, type of procedure, and location of procedure
    - Name, route, site, time of administration, and dosage of all medications
  - During the procedure
    - Record heart rate, blood pressure, oxygen saturation, and end-tidal CO_2 every 5-10 minutes
  - Following the procedure
    - Identical to those documented during the procedure, until patient awakens; intervals may then be spaced until patient returns to baseline level of consciousness
- **Rescue equipment**
  - Suction
  - High-flow oxygen source/supply (eg, bag-valve mask)
  - Vascular access equipment (especially if the patient is being sedated with IM medication)
  - Airway management equipment (oropharyngeal airway/nasal trumpet, laryngoscopes, endotracheal tubes, laryngeal mask airway, etc)
  - Resuscitation medications (rapid-sequence intubation medications, IV fluids, etc)
  - Reversal agents (if applicable)
  - Defibrillator/transcutaneous pacemaker

Abbreviations: ACLS, advanced cardiovascular life support; IV, intravenous; IM, intramuscular; PALS, pediatric advanced life support.

Preprocedural Fasting

There has been controversy regarding procedural sedation and preprocedural fasting. Currently, the ASA recommends a period of 2 hours after ingestion of clear liquids, 4 hours after breast milk, and 6 hours after solids. These guidelines are based on expert consensus and extrapolated data in which patients received sedation at the level of general anesthesia. As a result, these guidelines for general anesthesia are not applicable to PSA in the ED. There have been numerous studies regarding preprocedural fasting for PSA, and none have demonstrated increased rates of serious adverse events with decreased fasting times.

In 2021, Stewart et al published a retrospective review of 2674 pediatric patients presenting to a pediatric ED who required procedural sedation for orthopedic interventions.[17] Primary outcomes were length of stay, time from admission to start of sedation, length of sedation, time from end of sedation to discharge, and adverse events. There was a statistically significant difference in the length of stay and time from admission to sedation when the ASA guidelines were adhered to, resulting in an approximately 80-minute longer length of stay in the ED. There were only 55 adverse events, including 17 patients who vomited, but none aspirated during the recovery phase.[17] A 2018 study of 6183 pediatric patients receiving procedural sedation observed 3284 patients who did not adhere to ASA preprocedural fasting guidelines, and the authors found no association between fasting duration and adverse events such as vomiting (odds ratio [OR], 1.00), serious adverse events (OR, 1.01), or any adverse event (OR, 1.00).[18]

Roback et al analyzed data on preprocedural fasting from a prospectively generated database comprising consecutive sedation events in children over a 7-year period. Although there were 2085 procedural sedations during that time, fasting times were documented in only 1555 patients. This study demonstrated that there was no significant difference in the incidence of adverse events among patients fasting 0-2 hours, 2-4 hours, 4-6 hours, or >6 hours, and there were no documented aspiration events.[19]

Capnography

Capnography is commonly used during procedural sedation in the ED. It is a simple way to allow clinicians to monitor respiratory events, such as respiratory depression, by continuously measuring the highest value of carbon dioxide exhaled with each breath and displaying it on the monitor as a waveform. Capnography can detect hypoventilation in 2 different ways: It can detect a decrease in respiratory rate (bradypneic hypoventilation) that will lead to a rise of end-tidal carbon dioxide ($ETCO_2$) levels >50 mm Hg. Capnography can also detect a decrease in tidal volume while the patient is maintaining a normal

respiratory rate (hypopneic hypoventilation), which leads to $ETCO_2$ levels that are decreased or normal. This is typically defined as an $ETCO_2$ <30 mm Hg or a decline >10 mm Hg. Hypopneic hypoventilation during PSA increases dead-space ventilation, which can lead to decreased minute ventilation and subsequent decrease in oxygenation. Therefore, if a patient is receiving supplemental oxygen, a pulse oximeter may not be able to detect subclinical respiratory depression, and capnography would be a more sensitive monitor of respiratory depression.[20]

The early recognition of respiratory depression is important during PSA, as it can help prevent loss of airway reflexes that can lead to an increased risk for aspiration. There have been few randomized controlled trials regarding capnography in the ED setting, but there are several nonrandomized and observational studies that suggest that capnography detects hypoventilation earlier than pulse oximetry and pulse rate alone in the setting of supplemental oxygen.

In the first ED observational study of 74 patients performed by Miner et al and published in 2002, 33% of the patients meeting criteria for respiratory depression were detected by pulse oximetry, whereas 100% were detected by capnography. A total of 47 patients were given supplemental oxygen. Of the 33 patients who had respiratory depression, 57.6% of them received supplemental oxygen. There was no correlation between capnography and provider observation, as measured by the Observer Assessment of Alertness/Sedation Scale.[21]

A 2010 randomized controlled study demonstrated that, out of 72 patients who were given propofol for procedural sedation, capnography was 100% sensitive for predicting hypoxia. This is because every patient who developed hypoxia first exhibited capnographic evidence of respiratory depression. All patients received 3 L/min of supplemental oxygen via nasal cannula. Physician interventions were also higher in the capnography group due to earlier recognition of respiratory depression.[22]

A 2015 randomized controlled study of 154 pediatric patients receiving procedural sedation demonstrated that capnography improved the timeliness of physician intervention during periods of hypoventilation.[23] There have been 2 meta-analyses that suggest that capnography is limited in preventing oxygen desaturation. In a Cochrane database meta-analysis of 1272 patients who required procedural sedation, there was a lack of convincing evidence to suggest that the addition of capnography to standard procedural sedation monitoring affected the rate of oxygen desaturation while on supplemental oxygen.[24] The second meta-analysis of 662 patients indicated that there was a lack of statistical evidence to support its clinical usefulness as part of routine care during procedural sedation.[25] Despite the findings in these 2 meta-analyses, since capnography is low-risk, is noninvasive, can detect respiratory depression earlier than pulse oximetry, and is low in cost, it is recommended by ACEP during procedural sedation.[4]

Pulse Oximetry and Oxygen Administration

Pulse oximetry and supplemental oxygen are used routinely during monitoring of a patient undergoing procedural sedation. Pulse oximetry is recommended by the ASA.[5] In a prospective observational study of ASA class III/IV patients receiving supplemental oxygen, pulse oximetry detected hypoxia (oxygen saturation <90%) in only 3 of 41 patients who had respiratory depression during procedural sedation.[26] The number of patients who had episodes of respiratory depression was not clinically significant and there were no other clinically significant complications. This study demonstrates that, although pulse oximetry is a reliable and important monitoring modality, it is not sufficient, alone, to monitor for respiratory depression.

Oxygen administration during procedural sedation is used more frequently, since most patients are monitored on capnography. The goal of supplemental oxygen is to increase oxygen reserves, thereby delaying or preventing the onset of hypoxia. However, increasing oxygen reserves through supplemental oxygen is not without risk. Patients who are given supplemental oxygen desaturate only after a prolonged period of apnea.[22] Adults and adolescents who are preoxygenated with 100% FiO_2 (fraction of inspired oxygen) and become apneic have around 6 minutes until they desaturate below 90%. In healthy children aged 2 to 12 years, this will decrease to 3 to 4 minutes.[15] Early recognition of respiratory depression is important to help prevent loss of airway reflexes and risk for aspiration. The warning sign for apnea will be detected on capnography first, while the pulse oximeter reading initially remains normal.

There have been 2 randomized controlled studies to determine whether oxygen administration prevents hypoxia during procedural sedation with propofol. One study used 3 L of oxygen via nasal cannula and a definition of hypoxia of ≤93% SaO_2 (arterial oxygen saturation). While the results were not statistically significant ($P = .3$), oxygen desaturation was decreased by 10% compared to the control group without supplemental oxygen. In this study, 27 of the 110 patients experienced $ETCO_2$ changes consistent with respiratory depression, but they never became hypoxic. Respiratory depression was identified in only 1 of these patients, further demonstrating the importance of capnography.[27] The other study used high-flow oxygen via a nonrebreather mask at 15 L versus oxygen administration by nasal cannula. They found that there was less hypoxia in the nonrebreather group versus the nasal cannula group (19% vs 41%; $P = .007$).[28]

Despite not finding any difference in the rate of respiratory depression, both studies demonstrated

that oxygen administration during procedural sedation decreased the number of hypoxic events and did not increase the number of adverse events such as aspiration or respiratory depression. Oxygen supplementation can permit patients to safely tolerate short periods of respiratory depression or apnea without the need for positive-pressure-assisted ventilation and its potential for gastric insufflation. Since oxygen is easily administered when capnography is used, ACEP and ASA recommend oxygen supplementation during procedural sedation. Supplemental oxygen is commonly avoided when capnography is not used, thus permitting pulse oximetry to provide a warning should interactive monitoring fail to detect ventilatory compromise.

Preprocedural Treatments and Adjuncts

Several preprocedural treatment options have been explored to optimize sedation conditions or supplement inadequacies of the chosen agent. Specific options include preprocedural sedatives and antiemetics; preprocedural opioids are often provided while resources for definitive treatment under PSA are being gathered. Evidence is mixed as to the efficacy of any specific adjunct.

Preprocedural Opioids

Preprocedural opioids are often part of the provision of compassionate care prior to PSA in the ED. It should be noted, however, that in limited studies dedicated to assessing the outcomes associated with preprocedural opioid administration, there is a predictably increased risk for complications, and appropriate preparations should be made. In a prospective study of 6295 children undergoing PSA, those who received preprocedural opioids had higher odds of oxygen desaturation, vomiting, and requirement for positive-pressure ventilation compared to those who did not, with increasing odds of complications when opioids were administered closer to the procedure start time.[29] The most frequently utilized PSA agent in the cohort was ketamine (67.7% of sedations), followed by ketamine-propofol (13.1%) and propofol-fentanyl (9.7%) combinations. Those who received opioids within 30 minutes prior to sedation had a 13.8% rate of desaturation and 12.0% rate of vomiting compared to about half these rates if administered >90 minutes before. Fentanyl had a decreased odds ratio for oxygen desaturation and vomiting compared to morphine.[29] ACEP guidelines suggest that, when feasible, to delay propofol administration until after the peak effect of whichever opioid administered has passed or to utilize a local analgesic.[15]

Preprocedural Sedatives

Regarding preprocedural sedatives, there is evidence for their benefit prior to administering ketamine for procedural sedation, in adults, at the potential expense of increasing recovery time. A 2019 double-blind randomized controlled trial compared 0.05 mg/kg midazolam IV, 5 mg haloperidol IV, or placebo administered 60 seconds prior to ketamine IV for PSA in the ED.[30] At 5, 15, and 30 minutes after primary PSA agent administration, they observed a decrease in the incidence of agitation of 38.9% (number needed to treat [NNT], 2.6) for midazolam and 44.3% (NNT, 2.3) for haloperidol, with increases in recovery time of 17 and 32 minutes, respectively. There was an overall null effect on provider satisfaction.[30]

A double-blind randomized controlled trial of 200 patients randomized to IV versus intramuscular (IM) ketamine (1.5 mg/kg IV or 4 mg/kg IM) with or without midazolam IV at a dose of 0.03 mg/kg, reported a decrease in the incidence of agitation of 17% (NNT, 6.0), and a higher level of patient satisfaction, but not provider satisfaction. A statistically significant increase in sedation time was not observed; however, it should be noted that the study was not powered to detect this endpoint.[31] In the ACEP guidelines on ketamine use in procedural sedation, pre-administration of benzodiazepines is described as "reasonable but nonmandatory."[32] Notably, no trial, to date, has demonstrated a trend toward decreased rates of recovery agitation in children.

Anticholinergics

Coadministration of atropine or glycopyrrolate has traditionally been recommended with ketamine PSA to mitigate hypersalivation and its associated risk for airway and respiratory events. A large meta-analysis in children found that when receiving atropine or glycopyrrolate with ketamine PSA, overall airway and respiratory adverse events were significantly higher than the group that did not receive these medications.[33] A secondary analysis of this study demonstrated that when anticholinergics were used during ketamine PSA, atropine was superior to glycopyrrolate, with fewer vomiting and fewer airway and respiratory adverse events. However, neither anticholinergic showed efficacy in decreasing overall airway and respiratory adverse events.[34] Given the lack of tangible benefit, the literature is not supportive of anticholinergic prophylaxis unless patients have an impaired ability to mobilize secretions.

Antiemetics

Ketamine-associated vomiting has been reported to occur in 3.8% to 28.4% of sedations, often in the recovery phase. Although it is not a serious adverse event, it does increase length of stay in the ED.[35] Vomiting is also common in the hours after ED discharge.[36] Limited literature suggests a mild benefit of ondansetron administered parenterally during procedural sedations in which ketamine was used. In a frequently cited double-blind randomized placebo-controlled trial of 255 children, Langston et al demon-

strated that IV ondansetron administration before PSA had an NNT of 13 for vomiting in the ED and NNT of 9 for vomiting in the 12 hours post PSA. These benefits seem more prominent in adolescents who have higher baseline rates of vomiting during dissociative sedation.[37] These findings were corroborated in a large pediatric cohort study.[38] Additionally, IM ketamine administration carries even higher rates of associated vomiting. Small studies have demonstrated up to a 30% incidence of vomiting, while larger studies have shown a lower occurrence of vomiting (7%).[36,39,40] In a trial published in 2020 by Nejati et al, coadministration of IM ondansetron reduced this rate from 30.7% to 14.3%.[41] IM metoclopramide and oral ondansetron do not seem to have significant effects when ketamine is administered IM.[39,42]

Treatment

For dosages for agents frequently used for ED PSA, **see Table 2, page 11**.

Opioids

Parenteral opioids are commonly used for painful procedures in the ED. An opioid alone is rarely optimal for PSA and is generally used for its analgesic properties only. Opioids are typically used during PSA in combination with a sedative-amnestic agent. Opioids exert their effect by binding to specific opioid receptors (primarily μ, κ, δ) in the central nervous system. The most regularly utilized opioid for PSA is fentanyl.

Fentanyl has many advantages as an analgesic agent for PSA, given its rapid onset of action, short duration of activity, favorable cardiovascular hemodynamic profile, and availability of a reversal agent. It rapidly crosses the blood-brain barrier, and its effect is felt in as little as 90 seconds. Fentanyl's duration of action lasts from 30 to 40 minutes, with a half-life of 90 minutes. These properties permit the administration of multiple small doses that can be titrated to the desired clinical effect. For procedural sedation, a single dose of 0.5 to 1 mcg/kg IV is often given before the sedating agent for its analgesic properties. The dose can be titrated upward every 1 to 2 minutes. Respiratory depression is more likely at higher doses or when it is given rapidly. Hypotension and bradycardia rarely occur. Chest wall rigidity and glottic spasm are unique to fentanyl and are usually seen only with high doses (>3-5 mcg/kg). In a prospective study of 89 neonates, all 8 patients who developed chest wall rigidity were able to be reversed by naloxone.[43]

Remifentanil differs from fentanyl in that the onset of action is almost immediate, and it has a half-life of 3 to 10 minutes. The typical dose for remifentanil is 0.05 to 0.1 mcg/kg/min IV infusion with supplemental 0.5 to 1 mcg/kg boluses. Remifentanil provides rapid, deep analgesia with minimal central nervous system depression. Because it is eliminated by nonspecific tissue esterases throughout the blood and tissues, its elimination is independent of hepatic or renal function.[44] Furthermore, it is hemodynamically neutral and does not accumulate with prolonged infusion, as with propofol. In a systematic review of 10 studies, 3 studies were performed in the ED, with 2 of these studies by emergency physicians. These studies demonstrated satisfactory PSA conditions when remifentanil was combined with propofol. This combination resulted in faster recovery and no complications were observed in the ED.[45] In a randomized, double-blind trial of 96 ED patients comparing remifentanil to fentanyl/midazolam, remifentanil had lower procedural time, lower failure rate, and lower pain during the procedure as well as higher patient satisfaction.[46]

Benzodiazepines

Benzodiazepines are classic sedatives utilized ubiquitously in the ED. In addition to their sedative properties, they also afford excellent amnesia and anxiolysis. They work at the GABA-A receptors, enhancing the inhibitor effects of gamma-aminobutyric acid on neuronal excitability, thereby decreasing excitatory signaling. Midazolam is the prototypical benzodiazepine. Sedation performed with longer-acting agents such as lorazepam and diazepam has also been reported and studied in a limited capacity with mixed results; overall, their pharmacokinetic profiles are not conducive to PSA in the ED.[47,48]

Midazolam has a rapid onset when administered IV, with peak effect at 5 minutes. The typical initial dose is 0.05 to 0.1 mg/kg IV. Duration of action is short, lasting <30 minutes in children when administered intranasally and <2 hours when administered IV.[49] Administration route is versatile, with oral, intranasal, IM, IV, and rectal formulations available. Not surprisingly, oral, rectal, and IM formulations have significantly more delayed pharmacokinetics and are thus less desirable for PSA in the ED. Lastly, a reversal agent exists in flumazenil should there be complications. (See the "Reversal Agents" section on page 12 for particular cautions on the use of flumazenil.)

Benzodiazepines afford no analgesia and therefore are frequently combined with an additional agent such as fentanyl. Additionally, in the pediatric population, paradoxical agitation occurs with surprising frequency, thought to be a downstream effect of inhibition of cortical restraint centers and a decrease in serotonin, thereby increasing aggression. In a meta-analysis published in 2016, of those studies that recorded the incidence, agitation occurred in 18.1% of cases.[50] This trend was not present in a sister meta-analysis of adult patients.[51] However, in adults, midazolam as a sole agent and in combination with opioids carries the highest risk for apnea, complicating 5.1% and 2.6% of cases, respectively. They also carry above-average risk for bradycardia

and hypotension.[51] Therefore, we envision few situations in which benzodiazepines should be used as first-line agents for moderate or deep sedation.

Nitrous Oxide

Nitrous oxide provides excellent analgesia due to its predictability and rapid onset. It is a gas that is combined with oxygen at concentrations of 30% to 70%, and the mouthpiece for administration is held by the patient. The depth of sedation varies with the concentration administered; <50% concentration administered as a sole agent delivers only minimal sedation effect.[5] When used at higher concentrations, it can cause deeper sedation. However, a prospective observational study demonstrated that concentrations up to 70% are safe in the pediatric population.[52] A prospective randomized study of children comparing oral midazolam, local anesthesia, and nitrous oxide for facial suturing found that regimens that included nitrous oxide were more effective in reducing distress and had fewer adverse reactions and shorter recovery times.[53] Because nitrous oxide rapidly diffuses into gas-filled pockets, it can worsen conditions such as pneumothoraces, chronic obstructive pulmonary disease, and middle ear effusions. If nitrous oxide is used, ensure that the delivery systems are in working order to prevent exposure for medical staff. A United States Centers for Disease Control and Prevention recommendation guide can be found at: https://www.cdc.gov/niosh/docs/2007-151/pdfs/2007-151.pdf?id=10.26616/NIOSHPUB2007151

Propofol

Propofol has gained popularity in recent years outside of the operating room and is now one of the preferred agents for PSA in the ED. Propofol's mechanism of action has not been entirely elucidated, but is thought to be through GABA-A receptor agonism and potentially reduced glutamatergic activity through NMDA blockade. Propofol is a lipophilic sedative-hypnotic agent with potent amnestic properties unrelated to any other known sedative. However, propofol does not have any analgesic effects. It is ultra-short-acting, with onset of action within 30 to 45 seconds and duration of action of 3 to 10 minutes, depending on the dose. Typical dosing is 0.5 to 1 mg/kg IV as the initial bolus and then subsequent 0.5 mg/kg aliquots as needed.[15] Due to its lipophilic nature, it acts as a medium for bacterial growth and has been associated with the occurrence of healthcare-related infections.[54] Based on limited evidence, it seems that the combination of opioids and propofol results in lower pain scores and less recall, with variably increased rates of respiratory depression. Combining propofol with benzodiazepines does not seem to afford any additional benefit.[5]

Propofol is a potent agent, ideal for the ED setting, boasting the most rapid onset and offset of all available agents. When compared to benzodiazepines, recovery time is significantly quicker.[5] Propofol also provides amnesia and anxiolysis, making it an ideal agent for brief, painful procedures such as reductions. Lastly, propofol has antiemetic properties, with the lowest rates of associated vomiting when compared to other sedatives, as well as one of the lowest rates of recovery agitation.[50,51]

When compared to other agents, propofol carries a higher risk for inducing hypotension, as well as respiratory depression, with relatively higher reported incidences of hypoxia and apnea.[50,51] Hypotension is especially prominent in volume-depleted patients and should be avoided in these scenarios. Pain upon injection is well described in the operative setting, although this is uncommonly encountered in the ED. Propofol infusion syndrome is a theoretical risk, but has never been reported in the ED population and has been reported exclusively in intensive care unit patients sedated on continuous infusions at high doses for several days.[15]

Ketamine

Ketamine is a popular agent for PSA and is the most utilized agent in the pediatric population.[55] It is a phencyclidine derivative and NMDA receptor antagonist, effectively "disconnecting" the thalamocortical and limbic systems, thereby dissociating the central nervous system from outside stimuli. At a threshold "dissociative" dose of 1 to 1.5 mg/kg IV, 3 to 4 mg/kg IM, or 6 to 9 mg/kg intranasal, ketamine induces a trancelike, cataleptic state that is not deepened by additional doses. It is the only clinically available agent utilized for PSA that does not exhibit a dose-response continuum.[32,56] Doses below the dissociative threshold may not provide the desired effect. These unique pharmacokinetic properties make ketamine a very safe agent for use in the ED.

In addition to the safety afforded by this binary, dissociative-versus-subdissociative dosing of ketamine, the agent has several additional desirable properties. Ketamine has innate analgesic effects, with peak reduction in pain scores equivalent to IV morphine.[57] It induces profound amnesia, as well. Additionally, ketamine inhibits the reuptake of catecholamines, accounting for its significantly lower rates of hypotension and bradycardia compared to propofol or a combination of benzodiazepine/opioids.[32,50,51]

Contraindications for Ketamine

The only absolute contraindications to the use of ketamine for PSA are age <3 months (due to a collection of case reports describing increased rates of apnea and laryngospasm in this age group), a history of schizophrenia, and allergy to ketamine.[32] In a large 2016 observational study published by the Pediatric Sedation Research Consortium reporting on seda-

tions performed with ketamine alone or ketamine in combination with an additional agent (eg, ketamine-midazolam, ketamine-propofol, etc), an increased rate of desaturation and apnea was observed in the 0- to 3-month age group compared to older children, although cases of laryngospasm and other serious adverse events were equivalent.[58] Additionally, among available agents for PSA, vomiting was the most common adverse event reported with IV administration of ketamine, with a reported incidence of 1.1% to 8.1% of sedations in children and 17% of adults. Incidence appears to increase with age >13 years and with IM administration.[38,50,51,58] Recovery agitation, or emergence phenomenon, is common, but not serious enough to be clinically meaningful in children, with a reported rate of 1.4% for serious episodes of agitation. In adults, reported rates vary greatly, from 0 to 30%.[32] Two well-conducted double-blind randomized controlled trials suggested that pre-administration of midazolam in adults can mitigate this risk.[30,31]

There is a large body of inconclusive evidence that has marred ketamine with a substantial number of relative contraindications. Ketamine increases oral secretions, which has been implicated in airway compromise. A randomized controlled trial of 140 children using a visual analog scale to categorize the magnitude of excessive salivation found that there were very few cases of hypersalivation that required any intervention beyond airway repositioning and suctioning.[59] An observational study of 1090 pediatric patients using visual analog scale also found hypersalivation to be extremely uncommon, and no advanced airway interventions were required.[60]

Extrapolating from literature on inhalational anesthetics, the risk for laryngospasm was 5.5 and 3.7 times higher, respectively, in children with upper respiratory infection or active asthma. Incidence of these laryngospastic risk factors as they relate to ketamine administration are unavailable, but caution is advised for these patients.

Ketamine's sympathomimetic properties can induce mild to moderate increases in heart rate and blood pressure; however, the literature regarding safety of administration in those with hypertension and cardiac disease is inconclusive. Caution is advised based on the theoretical risk for dangerously increasing myocardial oxygen consumption in susceptible patients. Notably, no cases of myocardial ischemia have ever been reported in emergency medicine literature. Thyroid disease and porphyria are relative contraindications for ketamine use, due to inconclusive reports of sympathetic hypersensitivity. There are also conflicting reports of increased intraocular pressure or increased intracranial pressure with the use of ketamine.[31,32] Head trauma is no longer a contraindication for ketamine use, based on increasing evidence of equivalent outcomes when utilizing ketamine in this scenario.[61]

Ketamine-Propofol or "Ketofol"

Combined ketamine-propofol administration, also known as "ketofol," deserves special mention, given its ubiquity in the literature and in academic conversation. The 2 agents theoretically complement the other's weaknesses: Ketamine induces dissociative sedation, has innate analgesic properties, and cardiorespiratory stability with hypertensive and tachycardic effects. In contrast, propofol is a potent sedative, without analgesic effects, which has rapid onset and antiemetic properties but can cause hypotension and respiratory depression.

The most commonly described method of dosing of ketofol is a ratio of ketamine to propofol of 1:1, although ratios of 1:3 or 1:4 are described as well. Agents are administered either in the same syringe or sequentially. Little current evidence exists to recommend one ratio over another. In a double-blind randomized controlled trial of 271 adults split into 3 groups, comparing efficacy and safety of PSA in the ED with propofol alone, 1:1 ketamine to propofol, and 1:4 ketamine to propofol, the only significant difference identified was an 8% to 10% higher rate of recovery agitation with the 1:1 combination.[62] Similarly, Ayatollahi et al conducted a double-blind randomized controlled trial in patients aged 10 to 50 years undergoing PSA for nasal fracture reduction with either 1:1 or 1:3 mixtures of ketamine to propofol. In the 1:1 mixture group, they observed 4 times the rate of vomiting and hallucinations as well as decreased rates of provider and patient satisfaction compared to the 1:3 admixture. However, the 1:1 admixture also required bag-valve mask utilization in half as many cases as in the 1:3 ratio.[63] If redosing of ketofol is required, rarely does the ketamine component need to be redosed; therefore, a reasonable strategy would be to start with 1:1 ratio and redose propofol as needed based on patient response.

In adults, there are a few meta-analyses comparing the efficacy and safety of ketofol against its constituent agents. In general, ketofol demonstrates an increased safety profile compared to either agent alone. A 2016 meta-analysis comprised of 18 randomized controlled trials compared ketofol to propofol for PSA.[64] Ketofol was uniformly superior to propofol, with a relative risk (RR) of 0.47 for respiratory complications requiring intervention; RR 0.41 for hypotension; and RR 0.47 for bradycardia. Propofol had a nonsignificant trend toward decreased psychomimetic complications (ie, emergence phenomena).[64] Bellolio et al similarly quote lower rates of apnea and hypotension compared to either agent alone.[51] These findings were corroborated in a meta-analysis of exclusively emergency medicine randomized controlled trials, although the data were fewer and less robust.[65] In a 2021 double-blind randomized controlled trial, ketofol in a 1:1 ratio demonstrated nearly half the rate of recovery agitation as compared to ketamine

alone.[66] Therefore, in adults, if institutional policies permit, based upon available data, ketofol is a preferable agent to either agent alone, particularly for patients predisposed to hemodynamic or respiratory instability.

Ketofol Use in Children

In children, the data are limited, but of that which are available, it is strikingly dissimilar to that in adults and highlights instead the safety of ketamine as a sole agent in the pediatric population. Bhatt et al's multicenter observational study of 6295 pediatric PSA occurrences in the ED found that, when compared to ketamine alone, ketofol administration carried 4-fold increased odds of serious adverse events (eg, apnea, hypotension, laryngospasm), 2-fold increased odds of significant intervention on the part of the sedation provider, and 2-fold increased odds of oxygen desaturation.[38] The Pediatric Sedation Research Consortium corroborated these findings in their published report of an observational cohort of 22,645 pediatric PSA occurrences with ketamine alone or with adjuncts. Propofol coadministration was associated with an OR of 1.79 for any adverse event and an OR of 5.36 for serious adverse events.[58] Notably, 2 meta-analyses have been conducted that include ketofol utilization compared to other medications, but both are extremely heterogeneous, making conclusions difficult, and they fail to adequately assess ketofol against its discrete constituent agents.[50,67] Therefore, based on limited data, ketofol cannot be routinely recommended in this population, compared to ketamine alone.

Etomidate

Etomidate is an ultra-short-acting, nonbarbiturate, carboxylated imidazole chemically unrelated to any of the aforementioned agents. It has garnered significant attention in the last 2 decades for primary use during PSA in the ED. Similar to other hypnotic agents, etomidate induces sedation via agonism of the GABA receptors in the central nervous sys-

Table 2. Routinely Available Agents and Dosages for Emergency Department Procedural Sedation[49]

Agent	Starting Dosage, Adult and Pediatric Patients	Onset (min)	Duration (min)	Advantages	Disadvantages
Fentanyl	1 mcg/kg IV	1-2	30-40	• Rapid onset • Short duration • Minimal CV effects	• Chest wall rigidity (when given rapidly in large doses) • Analgesic properties only
Remifentanil	0.05-0.1 mcg/kg/min IV infusion with supplemental 0.5-1 mcg/kg IV boluses	<1-3	3-10	• Short duration • Can be titrated	• Respiratory depression • Analgesic properties only
Midazolam	0.05-0.1 mg/kg IV	1-5	60-120	• Rapid onset • Short duration • Multiple routes	• Respiratory depression • Moderate duration • Sedative properties only
Nitrous oxide	30%-70% concentration	1-2	3-5	• Rapid onset • Minimal CV effects	• Emesis • Expansion of gas-filled structures
Propofol	0.5-1 mg/kg IV	<1	3-10	• Rapid onset • Antiemetic • Short duration	• Hypotension • Respiratory depression • Injection pain • Sedative properties only
Ketamine	1-1.5 mg/kg IV 4-5 mg/kg IM 6-9 mg/kg IN (adults only)	~1 (IV) ~5 (IM)	10-15 (IV) 15-30 (IM)	• Preserved airway reflexes • Predictable • Provides analgesia and sedation	• Emergence phenomena • Emesis • Laryngospasm • Hypertension, tachycardia • Increased secretions
Ketamine-propofol (ketofol) (adult patients only)	1:1 admixture dosing: 0.5 mg/kg ketamine IV and 0.5 mg/kg propofol IV, administered simultaneously IV	1-3	10-15	• Airway preservation • Hemodynamic stability • Rapid recovery • Use together offsets hemodynamic effects of each individual agent • Provides analgesia and sedation	• Same as for each individual drug
Etomidate	0.15 mg/kg IV	<1	5-10	• Rapid onset • Minimal CV effects	• Respiratory depression • Myoclonus • Sedative properties only

Abbreviations: CV, cardiovascular; IM, intramuscular; IN, intranasal; IV, intravenous.

tem.[68,69] Typical dosing of etomidate is 0.15 mg/kg IV, and onset of action of etomidate is rapid, at 30 to 60 seconds, as is recovery, which occurs within about 5 to 10 minutes. Notably, etomidate has no analgesic properties and should probably be combined with opioids when analgesia is needed, although the literature is silent on whether concurrent analgesic administration affords any benefit.

Rates of adverse events with etomidate utilization are low, although dedicated studies in the ED are sparse and limit commentary. Based on the best available evidence, rates of hypotension and hypoxia are low, approximately half that of its ultra-short-acting alternative, propofol. Observed bradycardia is reported more frequently than with alternative agents, with 2 meta-analyses summarizing ED PSA reporting this adverse side effect in 9 of 194 adult and 4 of 60 pediatric sedations.[50,51] Rates of apnea are likely low, with one double-blind randomized controlled trial of 105 adults who received etomidate reporting a rate of 3.8%.[70]

Etomidate use is limited chiefly by its duration of action, often requiring redosing, as well as its well-described propensity to cause mild to severe myoclonus in 20% to 40% of sedations conducted in the ED, potentially hindering procedure completion.[4,70] Additionally, etomidate's unique side effect of adrenal suppression has historically been of concern; however, numerous studies examining cortisol levels and clinical sequelae after a single dose of etomidate for rapid sequence intubation have failed to demonstrate a clinically significant effect.[4]

Reversal Agents

Naloxone

Naloxone is a competitive antagonist of opioids and has a rapid onset of action. Although the half-life is around 45 minutes, its clinical effects last only about 15 to 30 minutes. Naloxone can be delivered IV, IM, intranasal, intraosseus, or via nebulizer, but during sedation, it is preferred to be given IV due to faster onset than other routes. It should be used only if there is significant respiratory depression due to opioid use alone. If using a short-acting agent such as fentanyl in PSA doses, re-sedation after naloxone wears off is generally not a problem. Partial reversal of opioids is more desirable than complete reversal so painful procedures can be continued once respiratory depression is reversed. There is no high-quality evidence to suggest the initial dosage of naloxone, but it can be anywhere from 0.04 to 0.2 mg IV and repeated every 1 to 2 minutes to the desired effect. Naloxone has been reported to cause pulmonary edema, dysrhythmias, and seizures.

Flumazenil

Flumazenil is a competitive antagonist of benzodiazepines. It is not as effective for reversing respiratory depression as it is for reversing the sedation effect. It has a rapid onset of action in 1 to 2 minutes and a peak effect in 5 to 10 minutes. However, the clinical duration is variable from 30 to 90 minutes, and thus re-sedation is possible in the setting of longer-lasting benzodiazepines. Flumazenil is administered in doses of 0.1 to 0.2 mg IV every 1 to 2 minutes to the desired effect. Flumazenil can provoke seizures in any patient, but more commonly in patients who are benzodiazepine-dependent, take tricyclic antidepressants, or have a history of seizures. The seizures can progress to status epilepticus that is refractory to common treatments. A double-blind randomized study of 179 patients receiving flumazenil versus placebo after PSA in the ED did not demonstrate any serious adverse events;[71] however, they studied only the time to return to baseline alertness and not the effect on respiratory depression. A meta-analysis of 13 randomized controlled trials demonstrated that flumazenil administration after benzodiazepine intoxication increased the risk for serious adverse events. Due to its unfavorable risk-versus-benefit profile, reversal with flumazenil is not recommended, except in limited situations.[72]

Special Populations

Pediatric Patients

Sedation in children is often used to relieve pain and anxiety as well as to modify behavior (eg, to induce immobility) to allow the safe completion of a procedure. Many brief procedures, such as minor laceration repairs, may be accomplished with distraction, local anesthesia, and topical anesthetics. Children younger than 6 years of age may be at greatest risk for an adverse event, since they are particularly vulnerable to the medication's effects on airway patency, respiratory drive, and protective airway reflexes. Studies have shown that it is common for children to pass to a deeper, unintended level of sedation.[73,74] A good working knowledge of and preparation for the use of rescue measures is therefore, essential in this patient population.[6]

The literature is divided on whether children aged <2 years have an increased risk for adverse events. In a meta-analysis of 8282 children aged <2 years receiving ketamine for procedural sedation, adverse respiratory and airway events were twice as prevalent as in older children. Although there were increased respiratory events such as laryngospasm, apnea, oxygen desaturation, and upper airway obstruction, no patients were ultimately intubated.[33] However, in a 2021 study, Schlegelmilch et al found no difference in the rate of adverse respiratory events in children aged 13 months to 2 years compared to older children.[75] In children who are <6 months of age (particularly <3 months old) and weighing <5 kg, there is a higher incidence of adverse events.[76,77]

Pregnant Patients

Minor traumatic injuries are common in pregnancy, often subsequently requiring painful diagnostic and therapeutic procedures. Pregnant women who are experiencing significant pain may benefit from PSA. There are several physiologic changes in pregnant women that affect procedural sedation. A decrease in blood pressure should be expected due to progesterone-induced vasodilation as well as aortocaval compression due to the gravid uterus. Furthermore, pregnant women have an increased risk for difficult intubation due to the mucosa of the upper respiratory tract becoming more vascular and edematous, which leads to swelling and increased risk for airway bleeding. Pregnant women also have an increased risk for reflux esophagitis, putting them at greater risk for aspiration.[78]

Midazolam, ketamine, opioids, and propofol can all be used for procedural sedation in pregnant women. In most instances, the exposure to the medications used in procedural sedation is brief, and the doses are relatively low; therefore, significant adverse pregnancy outcomes are not expected. There is conflicting evidence on whether benzodiazepines increase the risk of teratogenicity. Although a 1998 meta-analysis demonstrated an increased risk in malformations during the first trimester, when they pooled the data from the cohort studies, there was not an increased risk for major malformations.[79] A study of 1979 infants exposed to benzodiazepines showed that the rate of congenital malformations was comparable to all births in the registry.[80] These studies were conducted in women who had repeated exposures to benzodiazepines. Opioids, such as fentanyl, are not teratogenic; however, they cross the placenta, but are rapidly metabolized and rapidly redistributed to the fetus. Although propofol can cause maternal hypotension, it has a dilating effect on the fetal placental blood vessels, which maintains appropriate umbilical blood flow.[81] There are no studies to suggest risk for teratogenicity of ketamine, but a small study from 1979 demonstrated dose-dependent uterine contractions at doses of 2 mg/kg IV or more during the first trimester.[81,82]

Elderly Patients

Elderly patients (aged >65 years) may be deemed to be at high-risk for procedural sedation in the ED. However, actual data suggest that the complication rate is similar to the adult population in general. A systematic review of more than 10,000 patients revealed that the complication rate for elderly patients was not significantly different from adult patients.[51] Despite these findings, because elderly patients generally have higher ASA scores, it is prudent to still take precautions when sedating this subset of patients.

Patients With ASA Physical Status Class ≥III

There is little evidence regarding ED procedural sedation in patients with a higher ASA class. A prospective observational study of 62 patients demonstrated similar rates of respiratory depression, hypotension, and airway interventions in patients with ASA classes of III and IV (ie, with "severe systemic disease" and "severe systemic disease that is a constant threat to life," respectively).[26] Additional studies did not demonstrate increased risk for complications in this patient population.[52,83] However, when using propofol in these patients, there is an increased risk for hypotension compared to etomidate, 17% and 11%, respectively.[26] Due to the limited number of studies in the ED, judicious use of sedation for these patients is required, and if deemed necessary, periprocedural analgesics and sedation agents should be carefully individualized. For example, etomidate can be used for patients with baseline hypotension (also consider ketamine); use propofol if limiting procedural length; and use etomidate for quick on/quick off. We would also recommend that optimal resuscitation be performed prior to starting the procedure.

Controversies and Cutting Edge

As the use of procedural sedation continues to increase in the ED, additional therapeutic options and monitoring strategies continue to be studied.

Dexmedetomidine

Dexmedetomidine has been suggested as a viable option for procedural sedation due to its sedative and anxiolytic properties. It was originally approved in 1999 by the United States Food and Drug Administration for sedation in intensive care unit patients, but has been approved for procedural sedation since 2008. It has an onset of action of 5 to 10 minutes, with peak effect within 15 minutes of administration. Dexmedetomidine is structurally similar to clonidine but with a shorter half-life (2-3 hours vs 15-17 hours). It is a highly selective alpha-2 adrenergic agonist that acts as a sympatholytic at the level of the medulla and locus ceruleus, and its analgesic properties are attributable to alpha-2 agonism throughout the central and peripheral nervous system.[84] Dexmedetomidine has been shown to have minimal to no effect on respiratory drive, but approximately 58.7% of pediatric patients in one study experienced hypotension, hypertension, or bradycardia.[85] A limitation to its use is that dexmedetomidine is approved for procedural sedation only if administered via a 10-minute infusion load followed by a maintenance infusion.[86]

Target-Controlled Infusion

A feasibility study published in 2020 used target-controlled infusion (TCI) of propofol for procedural sedation in patients requiring shoulder reduction.[87]

They targeted a Modified Observer's Assessment of Alertness/Sedation Scale (OAA/S) score of 3 and were able to successfully reduce all 20 patients using propofol TCI without a reported adverse event. Patient satisfaction was documented in 14 patients, mean ± standard deviation of 97 ± 9 and time to sedation was 25 ± 8 min. Typically, time to sedation with bolus use of propofol is shorter.[15]

Bispectral Index System

A few studies have suggested using bispectral index (BIS) to more accurately monitor patients during procedural sedation. The BIS system uses processed electroencephalographic signals to measure sedation on a unitless scale from 0 to 100 (with 0 indicating coma and 100 indicating normal). A 2003 prospective study found that BIS reliably predicted patients undergoing procedural sedation and analgesia who were sedated to the point of general anesthesia from those with lesser degrees of sedation but did not discriminate mild-to-moderate sedation or moderate-to-deep sedation, as measured by the Ramsay Sedation Scale score.[88] Another study found titrating propofol to a BIS of 45 achieved adequate sedation in all patients, with no reported adverse outcomes.[89] BIS may be an adjunct monitoring strategy that can reduce adverse outcomes in procedural sedation.

Peripheral Tissue Oxygen Saturation Monitoring

Another prospective study monitored changes in peripheral tissue oxygen saturation (StO_2) during procedural sedation by using near-infrared spectroscopy monitors on the patient's thenar eminence.[90] They found that patients with respiratory depression and the use of supportive airway measures had greater changes in StO_2 during procedural sedation than patients who did not. This suggests that peripheral tissue oxygen saturation monitoring may be a useful tool for assessing respiratory adverse events in patients undergoing procedural sedation in the ED.

Disposition

After completion of the procedure with sedation, re-evaluation of the patient should be performed. Although there is a paucity of data regarding when to discharge a patient, generally accepted guidelines are to ensure that the patient is back to baseline mental status, has normal vital signs, and is tolerating oral hydration without any episodes of emesis.[6] A prospective study of 1367 pediatric patients who received sedation in the ED noted that serious adverse effects were uncommon after 25 minutes from the final medication dose, and determined that discharge was safe if there were no serious adverse effects during the procedure.[91] Patients who receive a reversal agent during sedation require a longer period of observation, because the duration of the drugs administered may exceed the duration of the antagonist, resulting in re-sedation.[6] Patients should be advised not to drive or participate in dangerous activities for 12 to 24 hours, should be ambulatory, and need to have a responsible adult to drive them home. Standard sedation discharge instructions should also be provided to the patient.

Summary

Procedural sedation is commonly used to reduce pain and anxiety associated with medical procedures performed in the ED. Successful outcomes are achieved when physicians appropriately determine the level of sedation required based on the complexity of the procedure being performed as well as the patient's risk factors for adverse outcomes. By utilizing the best combination of sedatives, dissociatives, and/or analgesic agents in a rapid and predictable manner, emergency clinicians can confidently perform urgent or emergent interventions and procedures without putting patients at significant risk for side effects. The correct physician staffing model, when used in conjunction with proper monitoring techniques and necessary adjuncts, can help ensure patients are kept safe.

Class of Evidence Definitions

Each action in the clinical pathways section of *Emergency Medicine Practice* receives a score based on the following definitions.

Class I
- Always acceptable, safe
- Definitely useful
- Proven in both efficacy and effectiveness

Level of Evidence:
- One or more large prospective studies are present (with rare exceptions)
- High-quality meta-analyses
- Study results consistently positive and compelling

Class II
- Safe, acceptable
- Probably useful

Level of Evidence:
- Generally higher levels of evidence
- Nonrandomized or retrospective studies: historic, cohort, or case control studies
- Less robust randomized controlled trials
- Results consistently positive

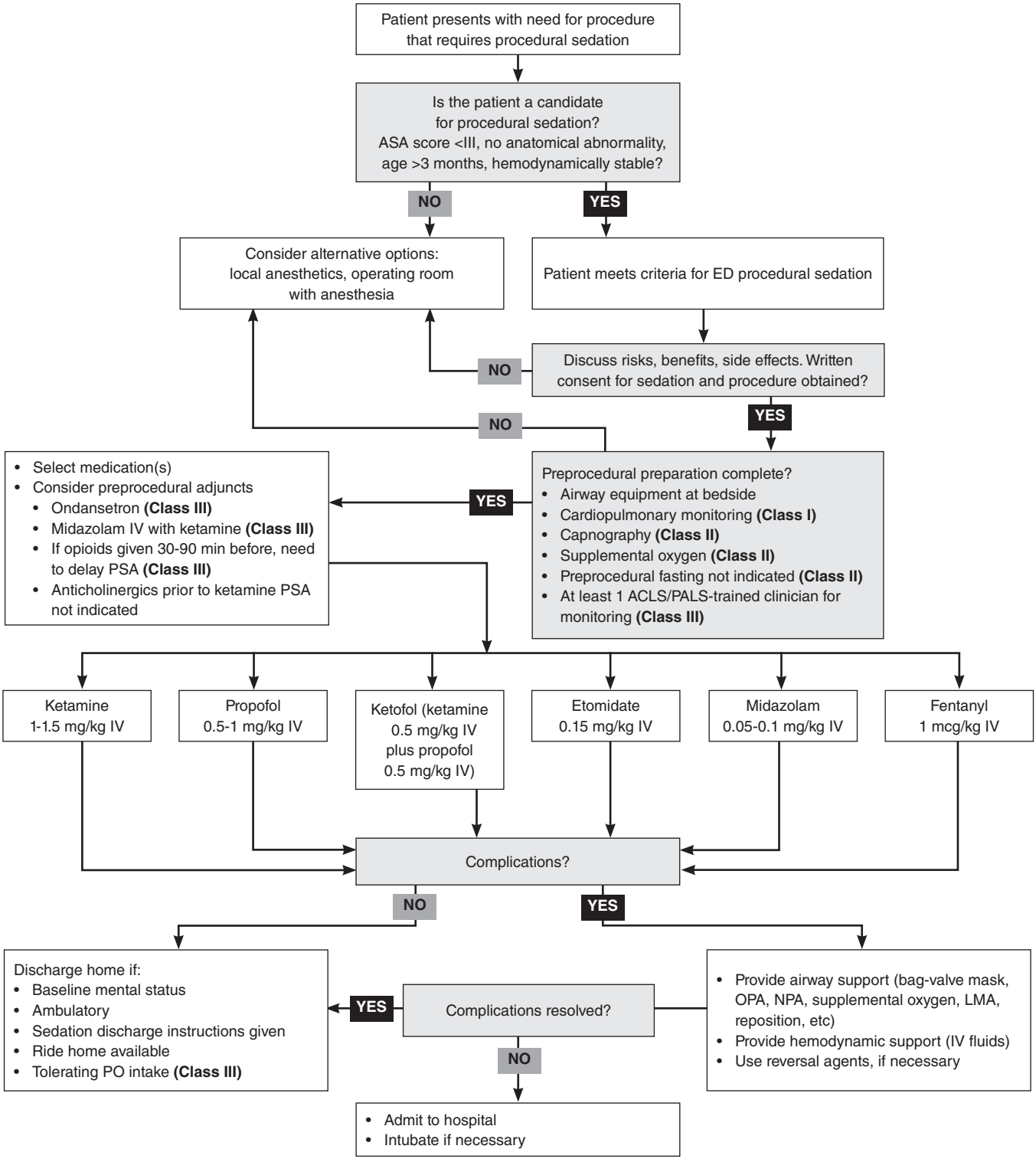
Class III
- May be acceptable
- Possibly useful
- Considered optional or alternative treatments

Level of Evidence:
- Generally lower or intermediate levels of evidence
- Case series, animal studies, consensus panels
- Occasionally positive results

Indeterminate
- Continuing area of research
- No recommendations until further research

Level of Evidence:
- Evidence not available
- Higher studies in progress
- Results inconsistent, contradictory
- Results not compelling

Clinical Pathway for Procedural Sedation and Analgesia in the Emergency Department



Abbreviations: ACLS, advanced cardiovascular life support; ASA, American Society of Anesthesiologists; ED, emergency department; IV, intravenous; LMA, laryngeal mask airway; NPA, nasopharyngeal airway; OPA, oropharyngeal airway; PALS, pediatric advanced life support; PO, by mouth; PSA, procedural sedation and analgesia.

For Class of Evidence Definitions, see page 14.

Case Conclusions

CASE 1

For the 30-year-old man who fell off a ladder and dislocated his shoulder…

After attempting to reduce his shoulder without sedation, you decided to perform procedural sedation to reduce his anteriorly dislocated right shoulder. After you consented the patient for procedural sedation and placed him on capnography, you decided to use 1 mg/kg of propofol IV immediately, without preprocedural fasting. The procedure went well, with adequate reduction of the right shoulder. You monitored him in the ED for 30 minutes until he was back to baseline mental status. You placed procedural sedation discharge instructions in his discharge papers, made sure he had a safe ride home, and discharged him.

CASE 2

For the 80-year-old man with congestive heart failure, hypertension, and diabetes with chest pain who needed cardioversion…

You determined that this patient was experiencing a congestive heart failure exacerbation, and that he was in ventricular tachycardia with a pulse. Despite being ASA class IV, the patient was in extremis and needed emergent cardioversion. Given that he was very ill and timely treatment was needed, it was appropriate to perform the procedure and the procedural sedation without another physician. After obtaining consent, you decided to use 0.15 mg/kg of etomidate IV, given its favorable hemodynamic profile. You placed the patient on pulse oximetry, capnography, oxygen via nasal cannula, and had rescue devices at bedside. The cardioversion was performed successfully, with return to normal sinus rhythm and an improvement of his blood pressure. Cardiology was consulted and the patient was admitted to the hospital.

CASE 3

For the 56-year-old obese woman who had multiple facial and leg lacerations…

The patient presented with multiple complex lacerations that required repair, but she appeared to be intoxicated, and she said she had a history of obstructive sleep apnea. Although most agents could be used safely, you decided ketamine was the best option for her, given that it preserves airway reflexes and has a favorable cardiopulmonary profile. You gave her 1 mg/kg ketamine IV and had available an additional 0.5 mg/kg in case she needed it. To prepare for any potential respiratory compromise, you pre-oxygenated her using nasal cannula and had rescue devices available at bedside. You monitored her respiratory status with pulse oximetry and capnography and checked her blood pressure every 5 minutes. She tolerated the laceration repair without complication, but she needed an additional dose of ketamine (0.5 mg/kg) for the procedure to be completed. She was observed for 1 hour after the last dose of ketamine. She called a friend to pick her up, and when she was ambulatory and tolerating oral intake, was discharged.

Time and Cost-Effective Strategies

- Always consider local anesthesia such as regional nerve blocks and intra-articular blocks prior to performing procedural sedation.
- Using IV medications rather than IM can shorten the ED length of stay.
- Using short-acting agents such as propofol can shorten the ED observation time after the procedure. A review article demonstrated that using propofol instead of midazolam reduced the ED length of stay and decreased cost.[92]
- PSA is much more cost-effective than admitting the patient for general anesthesia in the operating room. Patients who received operative management had an increased length of stay (50.4 hours vs 13 hours) and increased mean procedural charge ($3878 vs $1500).[93]
- Based on evidence, there is no need for preprocedural fasting prior to procedural sedation in the ED, which reduces disposition time.
- Although each hospital has its own protocol, it is appropriate to use only 1 physician to perform the sedation and procedure if no other physician is available to assist.

5 Things That Will Change Your Practice

1. Preprocedural fasting is not necessary.
2. Capnography is the best way to monitor respiratory depression.
3. Only 1 physician is needed for performing the sedation and procedure.
4. The clinical situation and patient history should guide the individual selection of medications for PSA in the ED.
5. Ketofol (ketamine and propofol) may be the best combination of medications for PSA for adult patients.

Risk Management Pitfalls for Procedural Sedation and Analgesia in the Emergency Department

1. **"The patient ate a full meal prior to coming into the ED, so I waited 6 hours to perform the procedural sedation."** Studies have demonstrated that preprocedural fasting is not needed in the ED. There have not been any increased events of aspiration or serious adverse events. In fact, preprocedural fasting causes a significant delay in disposition time without a benefit to outcome.

2. **"I needed to perform the procedural sedation as soon as possible, despite the patient's high ASA class or anatomic and physiologic abnormalities."** Prior to performing the procedure, an ASA class and a detailed airway examination should be performed to determine whether the patient has any comorbidities or anatomic variations that would put them at risk for difficult ventilation or airway compromise. If the ASA class is ≥III or there is concern about potential airway compromise, consider holding off on performing the procedure or consult anesthesiology.

3. **"I consented the patient for the procedure and thought that was sufficient."** The patient needs to be consented for the procedure and the procedural sedation. Both the procedure and the sedation have their own specific risks that need to be discussed with the patient. The physician, patient, and a witness need to sign the consent.

4. **"I didn't consider regional anesthesia."** Although procedural sedation is extremely safe in the ED, always consider regional or local anesthesia and intra-articular blocks prior to performing procedural sedation. Remember that nerve blocks, such as a scalene block, also have risks of their own.

5. **"I didn't use capnography because I thought I could safely monitor the patient using my visual assessments combined with the cardiac monitor and pulse oximetry."** Despite evidence that suggests that capnography is not mandatory, capnography can detect hypoventilation and hypoxia sooner than pulse oximetry alone. ACEP guidelines suggest the use of capnography during procedural sedation.

6. **"I thought I could monitor the patient and perform the procedure without needing another healthcare clinician."** There is no clear evidence to suggest that a 2-physician model prevents catastrophic events. It is appropriate to have 1 physician performing the procedure while a nurse or an advanced practice provider is monitoring the patient. In an ideal situation, it would be beneficial for another physician to be available to assist with the procedural sedation as you are performing the procedure.

7. **"I thought it would be okay to proceed with procedural sedation in this child despite his having received opioids."** Children who have received opioids within 30 minutes of the procedural sedation have a higher risk for oxygen desaturation, vomiting, and requirement for bag-valve mask ventilation. It is suggested that you delay procedural sedation until the peak effect of the opioid has passed.

8. **"The patient was 66 years old, so we decided not to offer procedural sedation for her painful procedure."** The complication rate for the elderly is not significantly different from other adult patients. Despite these findings, since the elderly generally have higher ASA scores, it is prudent to still take more precautions when sedating this subset of patients.

9. **"To prevent hypersalivation, I prophylactically treated the child with glycopyrrolate prior to giving ketamine for PSA."** Although coadministration of atropine or glycopyrrolate has been traditionally used with ketamine PSA, the literature suggests that these medications can actually increase airway and respiratory adverse events. Anticholinergic prophylaxis should be considered only in patients with an impaired mobility to mobilize secretions.

10. **"You must give medications through an IV for procedural sedation."** While most patients receive medications for procedural sedation through an IV, it is not uncommon to use intranasal or IM medications in certain instances, such as in pediatric patients. It is recommended to obtain IV access to treat complications and administer reversal agents, if necessary.

References

Evidence-based medicine requires a critical appraisal of the literature based upon study methodology and number of subjects. Not all references are equally robust. The findings of a large, prospective, randomized, and blinded trial should carry more weight than a case report.

To help the reader judge the strength of each reference, pertinent information about the study, such as the type of study and the number of patients in the study is included in bold type following the references, where available. The most informative references cited in this paper, as determined by the authors, are noted by an asterisk (*) next to the number of the reference.

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1. What level of sedation corresponds to a depressed level of consciousness where the patient cannot be easily aroused, but responds purposefully after repeated or painful stimulation?
a. General anesthesia
b. Moderate sedation
c. Minimal sedation
d. Deep sedation

2. For ED patients who require procedural sedation, how many hours should elapse after a full meal before the procedure can be safely performed?
a. 0 hours
b. 2 hours
c. 4 hours
d. 6 hours

3. Which monitoring modality detects respiratory depression first?
a. Pulse oximetry
b. Physician monitoring
c. Capnography
d. Cardiac monitoring

4. What medication decreases the incidence of emergence phenomenon when using ketamine for procedural sedation and analgesia?
a. Fentanyl
b. Zofran
c. Midazolam
d. Diphenhydramine

5. Which agent used for procedural sedation has shortest duration of action?
a. Ketamine
b. Propofol
c. Midazolam
d. Etomidate

6. What is a common side effect of propofol?
a. Laryngospasm
b. Hypotension
c. Nausea/vomiting
d. Tachycardia

7. What is ketamine's mechanism of action?
a. NMDA antagonist
b. GABA agonist
c. Mu receptor agonist
d. NMDA agonist

8. What is an absolute contraindication to using ketamine for procedural sedation?
a. Head trauma
b. Age <3 months
c. Coronary artery disease
d. Severe hypertension

9. Ketofol is most commonly given in which ratio of ketamine to propofol?
a. 1:1
b. 1:2
c. 1:3
d. 1:4

10. Which drug most commonly causes myoclonus?
a. Ketamine
b. Midazolam
c. Propofol
d. Etomidate

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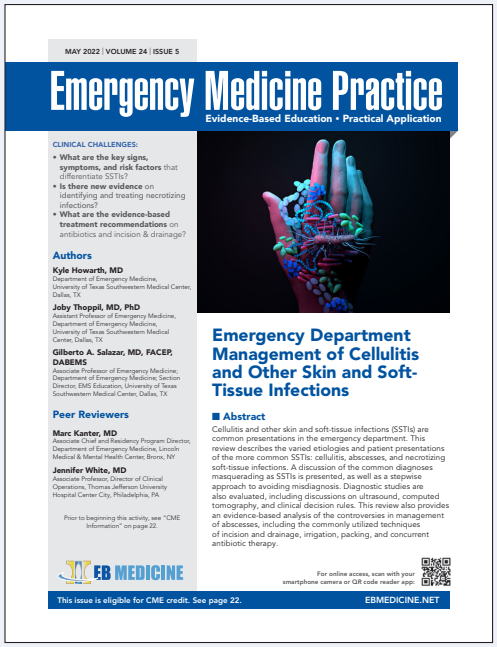

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Needs Assessment: The need for this educational activity was determined by a practice gap analysis; a survey of medical staff, including the editorial board of this publication; review of morbidity and mortality data from the CDC, AHA, NCHS, and ACEP; and evaluation responses from prior educational activities for emergency physicians.

Target Audience: This enduring material is designed for emergency medicine physicians, physician assistants, nurse practitioners, and residents.

Goals: Upon completion of this activity, you should be able to: (1) identify areas in practice that require modification to be consistent with current evidence in order to improve competence and performance; (2) develop strategies to accurately diagnose and treat both common and critical ED presentations; and (3) demonstrate informed medical decision-making based on the strongest clinical evidence.

CME Objectives: Upon completion of this activity, you should be able to: (1) identify patients who will benefit from procedural sedation and analgesia (PSA); (2) describe the mechanisms, risks, benefits, and doses of commonly used medications for PSA; (3) explain the use and algorithmic model for rescue therapy in the event of patient complications; (4) summarize the evidence on preprocedural fasting; and (5) discuss the evidence on monitoring modalities used during PSA.

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QUICK READ

Points & Pearls

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Procedural Sedation and Analgesia in the Emergency Department

Points

- Depth of procedural sedation and analgesia (PSA) should be tailored to (1) the procedure, (2) the needs of the patient, and (3) the risk tolerance level.
- Consensus guidelines suggest an increased risk for adverse events in patients who are at extremes of age; have difficult neck, pharyngeal, or facial anatomy; and/or underlying disease.
- A patient should be asked about any previous experiences with sedation/anesthesia, medication allergies, current drug and alcohol use, medications, and underlying medical conditions that might augment drug metabolism.
- The Mallampati score is insensitive for predicting difficult airway management.[11]
- Written informed consent for both the procedure and the procedural sedation should be obtained and documented.
- **See Table 1** for a preprocedural checklist for procedural sedation.
- The laryngospasm notch pressure may reverse laryngospasm. **See Figure 2**.
- Multiple observation studies have found no difference in adverse events with 1 physician/1 nurse and 2 physician/1 nurse models.[4-6,12-16]
- Randomized and observational studies suggest that capnography detects hypoventilation earlier than pulse oximetry and pulse rate alone in the setting of supplemental oxygen.[20-25]
- ACEP guidelines suggest delaying propofol administration until after the peak effect of an opioid has passed, or a local analgesic should be used.[5]
- Preprocedural sedative administration prior to ketamine may increase recovery time.[30-32]
- Head trauma is no longer a contraindication for ketamine use.[58]
- The literature is not supportive of anticholinergic prophylaxis unless the patient has an impaired ability to mobilize secretions.[33,34]
- Remifentanil was shown to have a lower procedural time, lower failure rate, lower procedure pain, and higher patient satisfaction.[43]

Pearls

- Complications for moderate and deep sedation were related largely to hypoxia that resolved with oxygen administration, bag-valve mask ventilation, or reversal agents.[12]
- Preprocedural fasting is not required for procedural sedation in the ED.[17-19]
- Although pulse oximetry is reliable and important monitoring modality, it is not sufficient, alone, to monitor for respiratory depression.[5,26]
- ACEP and ASA recommend oxygen supplementation during procedural sedation.
- Limited literature suggests a mild benefit for ondansetron administered parenterally when ketamine is used.[35,37]
- An opioid alone is generally used only for analgesic properties.
- Chest wall rigidity and glottic spasm are unique to fentanyl and usually seen only with high doses (>3-5 mcg/kg).[40]
- Administration of naloxone for reversal should be used only if there is significant respiratory depression from opioid use alone.
- Reversal with flumazenil is not recommended due to risk for adverse events.[68,69]
- Propofol has no analgesic effects, provides amnesia and anxiolysis, antiemetic properties, and the lowest rate of recovery agitation.[47,48]
- Ketamine has significantly lower rates of hypotension and bradycardia compared to propofol or benzodiazepine/opioids.[32,47,48]
- Although there is limited evidence on ketofol ratios, a 1:1 ratio is reasonable.[59,60]
- Ketofol is not recommended in pediatric patients, due to conflicting study results.[36,55,47,64]
- Patients who receive a reversal agent require longer periods of observation before discharge.
- For patients with an ASA class of ≥III, preprocedural analgesics and sedation agents should be carefully individualized.

