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Procedural Sedation

Introduction

Procedural sedation is an important skill for emergency physicians to possess to mitigate the patient's intense physical and emotional reactions to painful and threatening procedures.[1-3] Sedation not only facilitates and expedites procedures, allowing for early recovery and discharge, but also improves overall patient satisfaction.[4,5] The skill needed to manage the airway, institute resuscitation measures, and provide critical care monitoring uniquely gives emergency physicians the necessary training to achieve the goals of procedural sedation — maximizing analgesia, amnesia, and anxiolysis, all while controlling behavior and preserving patient safety.

The Spectrum of Sedation

Sedation is a continuum of progressive impairment of consciousness and inhibition of neuromuscular function that ranges from wakefulness to general anesthesia.[6-8] (*See Table 1.*) Minimal sedation causes mild cognitive and coordination impairment (e.g., ptosis and slurred speech). Patients with moderate sedation are somnolent but easily aroused with a light touch or voice. Minimal and moderate sedation are appropriate for procedures requiring only anxiolysis and analgesia. Deep sedation puts patients in a more profound level of somnolence in which they still purposefully respond to painful stimuli. Importantly, withdrawal from painful stimuli is not considered a purposeful response. With general anesthesia, the patient is unarousable to repeated painful stimuli and will likely require assistance with ventilation and maintaining a patent airway.

The dissociative agent ketamine is considered separately, as it causes a trance-like cataleptic state with profound amnesia and analgesia, all while preserving airway protective reflexes and respiratory drive.

Achieving the appropriate level of sedation creates a clinical challenge due to the wide variability in patient response to different agents. The divisions among the different levels of sedation are arbitrary, and individual patient reactions to sedation may not fit perfectly into one of the defined levels. Movement between levels of sedation can happen quickly and often at unexpected doses in some patients. As patients advance to deeper levels of sedation, they are at greater risk for cardiorespiratory compromise.[9,10] The emergency physician must be prepared to provide the necessary resuscitative measures should the patient inadvertently progress to a level of sedation that is deeper than intended.

Inadequate Sedation

Ideally, all painful procedures can be facilitated by using some level of sedation. However, there is a wide practice variation in sedation strategies, and patients in the emergency department are often under-sedated for some of the most painful procedures. Shavit and colleagues surveyed pediatric emergency physicians and found that less experienced physicians were less likely to use sedation and preferred restraints alone for the hypothetical case of a 3-year-old with a facial laceration who had already failed to achieve analgesia and

Executive Summary

- The ideal patient for ED procedural sedation is a previously healthy individual who requires an urgent, brief, but painful procedure.
- Patients with significant co-morbidities are best sedated in the OR.
- Pre-procedure preparation reduces the risk of adverse events and facilitates response should one occur.
- Supplemental oxygen reduces the incidence of hypoxemia, but delays recognition of hypoventilation.
- Drug combinations, especially with midazolam, are associated with increased incidence of adverse reactions.

anxiolysis with LET and distraction.[11] Inadequate use of analgesia has been identified in emergency medicine, especially when treating the most vulnerable of populations, namely children and the elderly.[12,13] Intubated patients often receive inadequate sedation in the emergency department[14] and are more likely to receive analgesics after being transferred early to an intensive care unit.[15]

Heath Care Policy, Quality Measures, Standards, and Guidelines

As the field of procedural sedation has expanded, regulating bodies have increased their oversight. The Joint Commission has set minimum standards for sedation, requiring consistent sedation policies within each individual institution, leaving the finer details of implementation to be determined at the individual hospital level.[16] These minimum standards stipulate that deep procedural sedation be provided by practitioners qualified to resuscitate patients if necessary, a skill every emergency medicine physician should possess.

There have been attempts to limit the use of deep sedation by non-anesthesiologists, often restricting the use of propofol and etomidate. In 2006, the American Society of Anesthesiologists declared that deep sedation should be limited to anesthesiologists, with no clear evidence to support this broad statement.[17] In 2009, the Center for Medicare and Medicaid Services (CMS) issued a statement stipulating that physicians administering deep sedation, namely propofol, not be involved in a simultaneous procedure. Fortunately, CMS later published a revised policy removing these restrictions and recognizing that propofol may be titrated to different levels of sedation. At least 27 sets of procedural sedation guidelines have been published since 1985,[18] and the controversy surrounding the regulation of procedural sedation continues. Fortunately, emergency physicians have the airway and resuscitation skills necessary to safely provide deep sedation in the emergency department.[19]

Patient Evaluation

The emergency physician should carefully consider whether or not the individual patient is a candidate for sedation in the emergency department or if the patient would be better served in the operating room. The type and duration of procedure that is planned may also help determine the most appropriate location for the procedure. Patient characteristics associated with the greatest risk of complication from procedural sedation include extremes of age (< 2 years and > 65 years),[20-24] significant airway abnormality, obstructive sleep apnea, morbid obesity,[25,26] hepatic or renal insufficiency, and American Society of Anesthesiologists (ASA) physical status classification of 3 or higher (*see Table 2*).[27] It is more challenging to appropriately dose sedative agents in groups with increased sensitivity to sedatives, altered pharmacokinetics, and/or skewed drug clearance.[28,29] The physician should perform a pertinent history and physical prior to sedation (*see Table 3*).[30] The emergency physician should also evaluate for potential difficulties with airway management. The mnemonics MOANS, SHORT, and LEMON (*Tables 4-6*) can be used evaluate the risks.[31-34] The physician should consider the potential of a difficult airway when deciding whether or not the patient is best served by ED sedation.

Fasting

The need for fasting prior to procedural sedation has been a topic of debate. The ASA recommends waiting two hours for clear liquids and six hours for solids before performing sedation; however, these recommendations are based on general anesthesia literature for elective cases in the operating room and not the emergency department setting.[30] In a review of 4,657 patients who had not been fasting according to the ASA guidelines, only 17 cases of vomiting occurred during ED sedation, with no evidence of aspiration.[35] Similarly, a prospective study enrolling 400 pediatric ED patients sedated with propofol, of which 282 had not fasted according to ASA standards, found only two patients with vomiting — one had fasted and one had not — and no episodes of aspiration.[36] A consensus guideline written by a panel of emergency medicine experts recommends prudent clinical decision-making on a case-by-case basis.[37]

Preparing for Sedation

Adequate preparation can help to mitigate risk and prevent adverse events from becoming catastrophic

Table 1: Levels of Sedation

Level of Sedation	Responsiveness	Airway Patency	Respiratory Drive	Examples
Minimal	Follows commands; Impaired cognition and coordination	Unaffected	Unaffected	Single dose pain or anxiety medication dose
Moderate	Purposeful response to light tactile stimuli	No intervention required	Spontaneous ventilations are adequate	"Conscious sedation"; adequate pain control with light sedation such as for abscess incision and drainage or shoulder reduction
Deep	Purposeful response to repeated or painful stimuli	May require intervention	Ventilatory function may be impaired	Level required for dislocated hip reduction, for example
General Anesthesia	Not arousable, even by painful stimuli	Requires intervention	Ventilatory function often impaired	General anesthesia for procedure such as rapid sequence intubation

(*see Table 7*). Almost half of all poor outcomes from procedural sedation are preventable, and standards and guidelines used for general anesthesia should be practiced for sedation care in any location.[38-40] In addition, several studies have emphasized that a dedicated team of trained professionals performing the procedural sedation improves outcomes.[20,41-43] Deep sedation may be accomplished either with the emergency physician monitoring the patient and a separate practitioner performing the procedure or by the same emergency physician both administering sedation and performing the procedure. Since ED procedures are typically brief and can be interrupted to address sedation concerns, it is common for deep sedation to be performed using a single emergency physician and an ED nurse. In these circumstances, the emergency physician will initiate effective sedation and, once stable sedation is established, the physician will perform the procedure while the nurse or other trained provider monitors the patient. The caveat is that the supervising practitioner performing sedation may also perform the procedure only if the procedure is of such a nature that it can be immediately halted should the patient suffer an adverse reaction that requires urgent attention or resuscitation.[18,27,44]

Table 2: Suitability for Sedation

ASA Class	Physical Status	Examples	Suitability for Sedation
1	No disease outside of uncomplicated surgical procedure	A normal healthy patient	Excellent
2	Systemic disease that is well controlled with no functional limitation	Mild or controlled asthma, diabetes, hypertension, anemia, epilepsy	Generally good
3	Severe systemic disease resulting in functional limitation	Moderate COPD, poorly controlled hypertension, diabetes with vascular complications, morbid obesity	Weigh benefits against risks
4	Severe systemic disease that is a constant life threat	History of angina, stroke, myocardial infarction or acute heart failure in the previous 6 months; sepsis; poorly controlled epilepsy	Benefits rarely outweigh the risks
5	Moribund patient who is not expected to survive without the operation	Septic shock, severe trauma	Extremely poor

Adapted from Krauss B, Green SM. Sedation and analgesia for procedures in children. *N Engl J Med* 2000;342:938-945.

Patient Monitoring

As the procedure progresses and the patient transitions between levels of sedation, close and continuous patient monitoring not only maintains patient safety but also guides repeat dosing. The designated professional responsible for patient monitoring must be able to clearly view the patient and assess for apnea, obstruction, emesis, or other problems. Monitoring is important during the procedure, and the same level of vigilance must be maintained until the patient has completely recovered. The period of time immediately following the procedure is often the most critical because of two factors.

Table 3: Pre-sedation Assessment

History	Past medical history, anesthesia history, history of snoring or sleep apnea, medications, allergies, fasting time, age, weight
Airway Exam	Mallampati score, obesity, neck size and mobility, micrognathia, edentulous, tonsillar hypertrophy (See Boxes 2-4)
Cardiovascular Exam	Heart rate, blood pressure, rhythm disturbances, distal pulses, carotid bruits
Respiratory Exam	Respiratory rate, pulse oximetry, obstructive lung disease, active upper respiratory infection

Table 4: MOANS: Difficult Bag Mask Ventilation

Mask seal: Beard, facial shape
Obesity: Increased upper airway tissue
Aged (> 55): Decreased upper airway muscle tone
No teeth: Difficult seal
Stiff lungs: COPD, asthma, CHF, and pulmonary fibrosis

Table 5: LEMON: Difficult Intubation

Look externally: Large teeth or tongue, short neck, small mandible
Evaluate 3-3-2 finger-breadths: Mouth opens 3, thyromental distance of 3, 2 from hyoid to thyroid cartilage
Mallampati score: Ability to visualize posterior oropharynx
Obstruction: Evidence of upper airway obstruction
Neck mobility: Immobilization due to cervical trauma or arthropathies

The first is the fact that once the painful stimulus is removed, many patients will slip into a deeper state of sedation. The second is that many times a medication will not reach its peak effect until after the procedure has been completed.

Supplemental Oxygen and Capnography

Despite research supporting the use of supplemental oxygen and capnography, there remains a practice gap in the utilization of these two techniques.[45,46]

Table 6: SHORT: Risk for Difficult Cricothyrotomy

Surgery scar
Hematoma
Obesity
Radiation
Tumor

Hypoxemia — one of the most significant complications of procedural sedation — can be prevented with supplemental oxygen. In healthy patients with normal cardiac output, the pulse oximeter oxygen saturation (SpO_2) reflects oxygenation delayed by 20 to 30 seconds.[47,48] In vasoconstrictive shock states, this lag extends up to 90 seconds.[49] Delayed drops in oxygen saturation are typically seen in hypoventilatory states because of this lag. However, if supplemental oxygenation is provided, hypoxemia can be prevented even during hypoventilation,[50] and it takes, on average, more than six minutes for a previously hyperoxygenated apneic adult to desaturate to below 90%.[51]

Thus, while oxygen supplementation prevents hypoxemia, it also obscures detection of severe hypoventilation, necessitating the use of continuous capnography. Capnography is more sensitive than clinical assessment or oxygen desaturation in detecting depressed ventilation.[52-56] Anesthesia guidelines suggest that capnography should be used in the setting of procedural sedation for patients with suspected sleep apnea because of the increased risk of airway obstruction.[57]

Noninvasive Positive Pressure Ventilation

The use of noninvasive positive pressure ventilation during procedural sedation has not been well studied. A case report describing its use in a morbidly obese patient with a history of obstructive sleep apnea who received procedural sedation with propofol for electrical cardioversion[58] suggests it may be a useful adjunct in patients at risk for upper airway obstruction.

Selecting Procedural Sedation Agents

When choosing sedation agents, match the desired depth and duration of sedation to the medication strategy. The depth chosen is specific to both the individual patient and the type of procedure. Patient factors include underlying illness, tolerance to medications, previous reactions to sedative agents, and idiosyncratic facets of pain. Moreover, different procedures involve different levels of painful stimuli.

The dynamic nature of procedural sedation can make achieving the appropriate level of sedation difficult. Some procedures involve an intense painful stimulus for a short period of time (e.g., shoulder relocation), followed by rapid-onset of relative pain relief. On the other hand, if the duration of the painful procedure exceeds the effective period of the sedative medication, the patient may become uncomfortable, increasing the risk of procedural failure and decreasing patient satisfaction and risking an unsuccessful procedure.

The ideal sedation agent should be easy to administer, predictable to titrate, fast in onset, short in duration, easily reversible, and inexpensive, all while maintaining cardiorespiratory stability and patient safety. Unfortunately, there is no perfect sedation agent or combination of agents for every patient or procedure. (*See Table 8.*) When sedation is administered, the practitioner should

Table 7: Procedural Sedation Checklist

- Informed consent for procedure and sedation
- IV access with IV fluid
- High flow oxygen through non-rebreather mask
- End-tidal CO2 monitor and pulse oximeter
- Blood pressure cuff cycling every 5 minutes at least
- Continuous EKG or telemetry (especially if at risk for cardiac disease)
- Cardiac Arrest Cart including defibrillator
- Airway equipment
  - –Suction equipment
  - –Bag valve mask
  - –Oral and nasal airways with lubricant
  - –Intubation equipment with appropriate ET tube
  - –Airway adjuncts such as supraglottic airways, bougie, surgical airway
- Rescue medications
  - –Additional sedation agents
  - –Naloxone
  - –Flumazenil
  - –Epinephrine
  - –Glycopyrrolate
  - –Phenylephrine
- Procedure timeout with sedation team, emphasizing roles in the sedation

attend closely to the dose, as well as the onset, peak, and elimination times for each agent. Ideal analgesic administration is before the onset of noxious stimuli from the procedure to allow for equilibrium based on peak onset times. Lastly, avoid using deeper levels of sedation as compensation for inadequate analgesia, and, whenever possible, use local and regional anesthesia to attenuate the need for systemic sedatives.

Dissociative Agent: Ketamine

Ketamine produces significant analgesia as well as a dissociative state characterized by unresponsiveness to nociceptive stimuli with cardiovascular stability as well as airway protection and respiratory drive.[59] Rapid onset and short duration are seen with intravenous administration and only slightly less so when given intramuscularly.[44] Emesis is more common with intramuscular as opposed to intravenous ketamine, but may be treated by premedication with ondansetron.[60] Other important but rare side effects include transient blood pressure elevation and laryngospasm.[44,61] Emergence reactions with ketamine are uncommon but may be associated with pre-procedural anxiety and can be treated and prevented with midazolam orally prior to the procedure.[44,62] Ketamine should be considered when intravenous access is not an option because the intramuscular dose is reliable and effective and it has an excellent safety profile.

Sedative-Hypnotics

Nitrous Oxide. Inhaled nitrous oxide provides sedation, anxiolysis, and mild analgesia with rapid onset and short duration for mild to moderately painful procedures. This drug allows for the patient to stay awake and follow commands; however, it often must be combined with opioid or local analgesia to achieve adequate sedation.[18] Vomiting is a common adverse effect of nitrous oxide, with no prevention by fasting.[63] Adverse events are more common in patients younger than 1 year of age and when used in combination with other sedatives.[22] The use of this agent requires special equipment, including a scavenger system to prevent occupational exposure, which is associated with infertility and spontaneous abortion.[64,65] The risk of vomiting, monitoring requirements, and availability of other options make nitrous oxide a substandard sedation option.

Dexmedetomidine. Although primarily used as an adjunctive agent in the critical care and perioperative setting in both adults and children, dexmedetomidine may be considered for procedural sedation in the emergency department.[66,67] Dexmedetomidine achieves hypnosis, anxiolysis, and analgesia as a potent alpha-2 antagonist (similar to clonidine) without causing respiratory depression.[59] It is typically given as a loading dose over 10 minutes, followed by infusion.[68] Onset is within minutes, with a very short duration due to rapid redistribution. Dexmedetomidine is most useful for quick emergent procedures, in patients with opiate tolerance, and in cases where respiratory depression would be unsafe. Because of its sympatholytic properties, dexmedetomidine's side effects include bradycardia and hypotension.

Etomidate. Etomidate is a short-acting agent that first was used for general anesthesia but has become useful for deep sedation at lower doses. Within seconds, it provides hypnosis, anxiolysis, and amnesia with a duration of 5 to 15 minutes.[69] Etomidate does not have any analgesic effects and often must be combined with analgesia (fentanyl is an excellent option). Key adverse effects include respiratory depression and emesis.[70] Myoclonus occurs in 20-45% of patients and is often mistakenly assumed to be seizure activity.[71] Myoclonus can be treated with midazolam in severe cases. Etomidate's temporary suppression of adrenal function has not been shown to have clinical significance for most ED patients, but is of some concern in ICU patients.[72]

Propofol. Similar to etomidate, propofol's quick onset, short duration, and easy redosing are ideal for procedural sedation. It also has beneficial antiemetic properties. Similar to etomidate, propofol does not have analgesic properties, and the addition of an analgesic may

Table 8: Medications

Drug	Effect	Elimination	Onset	Duration	Dosing	Pros	Cons
Ketamine*	Dissociative Amnesia	Renal	1 min IV 5 min IM	10-20 min	1-2 mg/kg IV; IV redose at 0.25-0.5 mg/kg every 5-10 min; 3-4 mg/kg IM	Preserves respiratory drive and airway reflexes	Sympathomimetic causes tachycardia and hypertension; Increases intracranial and intraocular pressure; emesis; Laryngospasm; Possible emergence reaction; Slightly increases secretions; Avoid in psychotic patients
Nitrous oxide	Hypnosis Mild analgesia Anxiolysis	Erythrocytes	3-5 min	3-5 min	50-66% N_2O/O_2	Very short duration Inhalation agent	Often requires second agent to achieve adequate sedation; emesis; Requires special apparatus; Occupational exposure associated with spontaneous abortions
Dexmedetomidine*	Hypnosis Anxiolysis Some analgesia	Hepatic	2-5 min	~ 6 min	Load 1 mcg/kg/min over 5-10 minutes then 0.2-1 mcg/kg/hr infusion	Very short duration Preserves respiratory drive and airway reflexes Sedates patients who are insensitive to benzodiazepines	Expensive Bradycardia Hypotension
Etomidate*	Hypnosis Some amnesia	Hepatic	< 1 min	5-15 min	0.1-0.2 mg/kg over 1 minute	Very short duration; minimal cardiovascular effects	Airway obstruction and respiratory depression; myoclonus; emesis; adrenal suppression No analgesia
Propofol	Hypnosis Some amnesia	Hepatic	< 1 min	3-10 min	0.5-1.0 mg/kg over 1-2 minutes or 0.5 mg/kg titrated in 20 mg aliquots to desired effect.	Short acting Anti-emetic	Airway obstruction and respiratory depression; Hypotension (consider infusion rather than bolus); Pain at injection site; Allergy: soy and egg No analgesia
Methohexital*	Hypnosis Anxiolysis Amnesia	Hepatic	< 1 min	15 min	0.75-1 mg/kg IV bolus and can be redosed at 0.5 mg/kg every 3-5 minutes; 25 mg/kg rectal	Shorter acting, inexpensive, can be given rectally for pediatric sedation	Airway obstruction and respiratory depression; Hypotension and cardiovascular depression; Laryngospasm; No analgesia
Pentobarbital	Hypnosis Anxiolysis Amnesia	Hepatic	15-60 min	1-4 hours	Rectal:< 4 years: 3-6 mg/kg; >4 years: 1.5-3 mg/kg, max 100 mg; Adults 100 mg slow IV bolus; peds 2-5 mg/kg IV	Longer acting Multiple routes of administration	Airway obstruction and respiratory depression Prolonged duration Slow recovery associated with agitation No analgesia
*Off-label use for procedural sedation							

be necessary. Multiple studies have shown that the use of propofol can shorten recovery time for orthopedic procedures, reducing overall ED length of stay.[73,74] In addition, in a prospective randomized trial comparing propofol and etomidate, propofol had a greater rate of procedural success and less myoclonus.[69] However, that same study also revealed a trend in which propofol caused more subclinical respiratory depression. Another common side effect is hypotension, which can be reversed with the short-acting alpha-1 agonist phenylephrine. Another adverse effect includes pain at the injection site. Nonetheless, propofol's positive attributes make it a very attractive option for many ED procedures.

Table 8: Medications (continued)

Drug	Effect	Elimination	Onset	Duration	Dosing	Pros	Cons
Midazolam	Hypnosis Anxiolysis Amnesia	Hepatic Active metabolite excreted renally	5-10 min (rectal); 3-5 min IV	1-4 hrs (rectal); 15-45 min IV; 1-2 hr IM	0.05-0.1 mg/kg IV (30-50% less in combo with opioid); Age greater than 70 years, half dose Age greater than 90 years, quarter dose	Reversal agent: flumazenil Shorter onset and duration than other benzodiazepines; Can be given intranasally	Airway obstruction and respiratory depression; Paradoxical excitement and disinhibition; Some hypotension; No analgesia
Alfentanil*	Amnesia Hypnosis at higher doses	Hepatic Active metabolite excreted renally	1 min	30-60 min IV	3-10 mcg/kg	Very short duration; less potent fentanyl; Reversal agent: naloxone	Minimal sedative effect; hypotension; hypoxemia; apnea; vomiting
Hydromorphone*		Hepatic	5-10 min	2-4 hrs IV	0.5-1 mg IV (Adult dose)	May work if patients are tolerant to morphine or fentanyl Reversal agent: naloxone	Histamine release
Morphine*		Hepatic Active metabolite excreted renally	5-10 min	2-4 hrs IV	4-8 mg (Adult dose)	Reversal agent: naloxone	Histamine release
Fentanyl*		Hepatic	1-2 min	30-60 min for single dose IV	0.5-1 mcg/kg every 1-2 min to effect	Less hypotension than other opiates; 100 times more potent than morphine; Reversal with naloxone	Minimal sedative effect; hypotension; hypoxemia; apnea; vomiting; chest rigidity when given fast
Flumazenil	Benzodiazepine receptor antagonist		1-2 min	30-60 min IV	0.1-0.5 mg		Rare agitation upon awakening Seizures, especially with chronic benzodiazepine users
Naloxone	Mu opioid receptor antagonist; reversal agent		1-2 min	20-40 min IV	0.04-0.5 mg		Hypertension Tachycardia Pain Diaphoresis
*Off-label use for procedural sedation							

Barbiturates

Barbiturate use in procedural sedation has declined dramatically with the rising popularity of etomidate and propofol. Methohexital, the most commonly used barbiturate, has a quick onset and short duration; however, it can precipitate seizures in a small percentage of patients.[18] Rectal use of methohexital is reliable and effective and may be an option in selected patients. Another attractive feature for methohexital is the extremely low cost compared to many other options. Pentobarbital is sometimes used for pediatric procedural sedation, but its long recovery time is associated with adverse effects, including agitation.[61]

Midazolam

When administered intravenously or intranasally, midazolam achieves hypnosis, anxiolysis, and amnesia within minutes and is usually eliminated within one hour.[61] When given orally, onset and duration are unpredictably prolonged due to first pass metabolism.[18] Midazolam can cause respiratory depression, hypotension, and paradoxical excitement.[24] Its effects can be reversed with flumazenil. The main disadvantage of midazolam is the extreme variability in patient dosing and effect. In addition, many pediatric patients will have a paradoxical increased agitation at recommended doses. Midazolam also has no analgesic properties, so it must be combined with an analgesic.

Opioids

Opioids are commonly used for sedation due to their analgesic properties as well as their ability to potentiate the effect of other sedatives. Fentanyl is the most commonly used opioid for procedural sedation because it has a short duration of action and less histamine release than either hydromorphone or morphine.[61] Compared with other opiates, fentanyl causes less emesis, pruritus, and hypotension. Respiratory depression, bradycardia, and hypotension are key adverse effects. Remifentanil and alfentanil are even shorter acting than fentanyl and will likely be used more commonly for short procedures in the future.[24] Naloxone reverses the effects of opiates.

Specific Combination Agents

Recent literature has called into question the broad use of midazolam with fentanyl.[1] Midazolam's slower onset and long duration of action have been shown to delay recovery, discharge home, and return to daily living.[75] Additionally, when combined with opiates, synergic hemodynamic and respiratory depression has been observed.[40] Along those same lines, the combination of benzodiazepines and opiates is associated with a greater risk of respiratory compromise than midazolam alone or midazolam with ketamine.[76] Lastly, multiple studies have provided further evidence emphasizing that the use of multiple sedative agents is associated with more frequent adverse events.[20,21,41,77,78]

Ketamine and Propofol. The combination of decreased doses of ketamine and propofol has become popular for procedural sedation. Theoretically, this combination agent should take advantage of the seemingly synergistic and complimentary effects of ketamine and propofol. Ketamine's association with the release of endogenous catecholamines should counterbalance the hypotension seen with propofol, and the antiemetic effects of propofol should prevent the emesis seen with ketamine.[79] However, the literature has yet to show a significant outcomes benefit with this combination.[80-85] Ketamine and propofol are typically combined as a 1:1 ratio (0.5 mg/kg each) in one syringe, but the ratio of the two drugs can be adjusted to target more sedation or dissociation.

Recovery and Discharge

Complications during procedural sedation are more likely to occur immediately after completion of the procedure and removal of the noxious stimulus. Observational studies of ED procedural sedation indicate that no adverse events were observed after 25 minutes had elapsed after the last sedative dose in children[86] and 12 minutes in adults.[87] Patient monitoring must continue until cardiorespiratory stability is ensured and the patient's mental status has returned to baseline.

Special Patient Populations

Pediatrics. Procedural sedation for children may be required prior to painless procedures such as diagnostic imaging. Controlling behavior becomes difficult in the face of heightened fear amplified by parental anxiety, strange environments, and the anticipation of pain. This fear, combined with the need to control behavior, often necessitates mild or moderate sedation.[88] Because children are easily overpowered and cannot withdraw consent, adequate analgesia becomes even more important.[89]

Both the pharmacokinetics and pharmacodynamics of procedural sedation drugs may differ in children.[61] Techniques such as desensitization (i.e., gradually increasing the painful stimulus over time), distraction (e.g., nonnutritive sucking with sucrose, playing a game, or watching a movie), and positive reinforcement from parents have all been shown to improve procedural sedation.[90,91]

Obesity. The anatomy and physiology of obese patients not only alters pharmacokinetics but also increases the risk of adverse events related to procedural sedation. Generally, obese patients have less total body water, larger adipose mass, relatively larger lean body mass, and greater glomerular filtration rates. This alters the pharmacokinetics of all drugs, especially lipophilic drugs such fentanyl and propofol with a greater volume of distribution. In addition, the greater redundant airway soft tissue of obese patients increases the risk of obstructive sleep apnea, which leads to obstruction during sedation.[26] Obese patients, even without obstructive sleep apnea, suffer from a greater risk of hypoxemia and airway obstruction during sedation.[92,93]

Elderly. Although many experts believe elderly patients have greater risk of adverse sedation events, the limited amount of research available has not validated this assertion.[94-95] It should be noted that elderly patients have increased sensitivity to all sedative drugs, especially opiates and benzodiazepines, and cautious titration is preferred.[24]

Discharge

Patients should not be discharged until they are alert and oriented to their baseline. They should have stable vital signs (consistent with their baseline) and be able to ambulate at their baseline. A responsible adult should be present to drive the patient home and stay with him or her for 6-12 hours. Patients and caregivers must be instructed to avoid eating or drinking for two hours after discharge and then to advance the diet slowly, starting with liquids as tolerated. Patients must avoid any activity that requires normal balance, strength, and coordination for 12-24 hours. Patients should not drink alcohol for 24 hours.

Take-home Points

Many patients in the ED will require procedural sedation. The emergency physician must be comfortable with multiple drug regimens and be able to adapt them to a given situation. Preparation and planning are the keys to preventing adverse

outcomes. If the physician is prepared to manage the patient's airway and resuscitate the patient, when necessary, prior to starting the procedure, almost all adverse outcomes can be avoided.

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Physician CME Questions

1. Which of the following statements is true?
   A. Propofol provides hypnosis, amnesia, and analgesia.
   B. It is appropriate to use a longer-acting sedation agent for quick procedures.
   C. Desensitization, distraction, and positive reinforcement can improve pediatric procedural sedation.
   D. Elderly patients do not require decreased dosing of sedation agents.

2. Which of the following is true?
   A. Capnography detects hypoventilation sooner than pulse oximetry.
   B. Capnography is not needed if you use supplemental oxygen.
   C. Moderate sedation is defined as impaired cognition and coordination, but the patient is able to follow commands.
   D. Age > 55 is not a risk factor for difficult bag ventilation.

3. The clinical manifestations of hypoventilation include which of the following?
   A. bradycardia
   B. arrhythmias
   C. agitation and confusion
   D. hypoxemia
   E. all of the above

4. Which of the following is an opioid?
   A. ketorolac
   B. ketamine
   C. alfentanil
   D. propofol

5. The most common causes of complications during procedural sedation include which of the following?
   A. inappropriate patient selection
   B. overmedication
   C. lack of monitoring during and after the procedure
   D. unanticipated adverse effects of sedation agents
   E. all of the above

6. In what ASA classification would you place a patient with COPD requiring oxygen at all times?
   A. ASA 1
   B. ASA 2
   C. ASA 3
   D. ASA 4
   E. ASA 5

7. Etomidate has all of the following properties *except*:
   A. It can induce myoclonus.
   B. It is an analgesic.
   C. It can cause adrenal suppression.
   D. It has a rapid onset.

8. Which patients are more likely to have complications during procedural sedation?
   A. obese patients
   B. elderly patients
   C. pediatric patients
   D. patients with chronic illness
   E. all of the above

9. Which of the following agents preserves respiratory drive and airway reflexes?
   A. propofol
   B. versed
   C. dexmedetomidine
   D. methohexital

10. Which of the following is true regarding opiates?
    A. No synergistic effects are seen when given with benzodiazepines.
    B. Respiratory depression may become less pronounced after stimulation from the procedure has ended.
    C. Hydromorphone is shorter acting than alfentanil.
    D. Chest wall rigidity is a known adverse effect of fentanyl.

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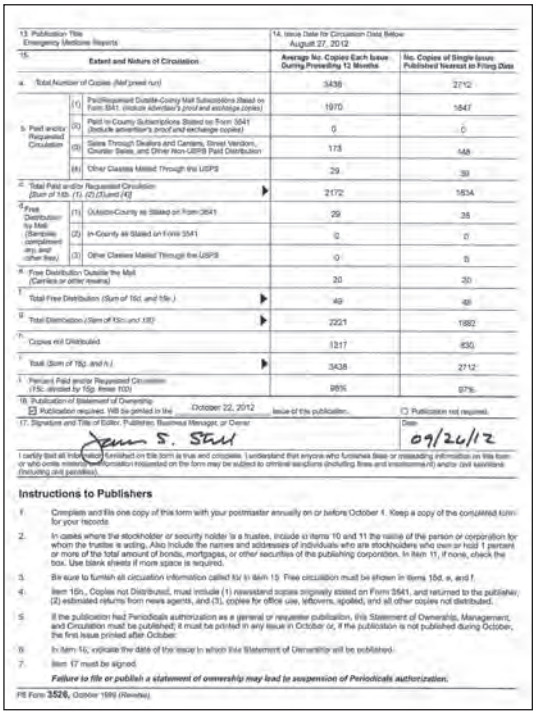

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Procedural Sedation

Levels of Sedation

Level of Sedation	Responsiveness	Airway Patency	Respiratory Drive	Examples
Minimal	Follows commands; Impaired cognition and coordination	Unaffected	Unaffected	Single dose pain or anxiety medication dose
Moderate	Purposeful response to light tactile stimuli	No intervention required	Spontaneous ventilations are adequate	"Conscious sedation"; adequate pain control with light sedation such as for abscess incision and drainage or shoulder reduction
Deep	Purposeful response to repeated or painful stimuli	May require intervention	Ventilatory function may be impaired	Level required for dislocated hip reduction, for example
General Anesthesia	Not arousable, even by painful stimuli	Requires intervention	Ventilatory function often impaired	General anesthesia for procedure such as rapid sequence intubation

Suitability for Sedation

ASA Class	Physical Status	Examples	Suitability for Sedation
1	No disease outside of uncomplicated surgical procedure	A normal healthy patient	Excellent
2	Systemic disease that is well controlled with no functional limitation	Mild or controlled asthma, diabetes, hypertension, anemia, epilepsy	Generally good
3	Severe systemic disease resulting in functional limitation	Moderate COPD, poorly controlled hypertension, diabetes with vascular complications, morbid obesity	Weigh benefits against risks
4	Severe systemic disease that is a constant life threat	History of angina, stroke, myocardial infarction or acute heart failure in the previous 6 months; sepsis; poorly controlled epilepsy	Benefits rarely outweigh the risks
5	Moribund patient who is not expected to survive without the operation	Septic shock, severe trauma	Extremely poor
Adapted from Krauss B, Green SM. Sedation and analgesia for procedures in children. *N Engl J Med* 2000;342:938-945.			

Procedural Sedation Checklist

- Informed consent for procedure and sedation
- IV access with IV fluid
- High flow oxygen through non-rebreather mask
- End-tidal CO2 monitor and pulse oximeter
- Blood pressure cuff cycling every 5 minutes at least
- Continuous EKG or telemetry (especially if at risk for cardiac disease)
- Cardiac Arrest Cart including defibrillator
- Airway equipment
  - –Suction equipment
  - –Bag valve mask
  - –Oral and nasal airways with lubricant
  - –Intubation equipment with appropriate ET tube
  - –Airway adjuncts such as supraglottic airways, bougie, surgical airway
- Rescue medications
  - –Additional sedation agents
  - –Naloxone
  - –Flumazenil
  - –Epinephrine
  - –Glycopyrrolate
  - –Phenylephrine
- Procedure timeout with sedation team, emphasizing roles in the sedation

Pre-sedation Assessment

History	Past medical history, anesthesia history, history of snoring or sleep apnea, medications, allergies, fasting time, age, weight
Airway Exam	Mallampati score, obesity, neck size and mobility, micrognathia, edentulous, tonsillar hypertrophy (See Boxes 2-4)
Cardiovascular Exam	Heart rate, blood pressure, rhythm disturbances, distal pulses, carotid bruits
Respiratory Exam	Respiratory rate, pulse oximetry, obstructive lung disease, active upper respiratory infection

Medications

Drug	Effect	Elimination	Onset	Duration	Dosing	Pros	Cons
Ketamine*	Dissociative Amnesia	Renal	1 min IV 5 min IM	10-20 min	1-2 mg/kg IV; IV redose at 0.25-0.5 mg/kg every 5-10 min; 3-4 mg/kg IM	Preserves respiratory drive and airway reflexes	Sympathomimetic causes tachycardia and hypertension; Increases intracranial and intraocular pressure; emesis; Laryngospasm; Possible emergence reaction; Slightly increases secretions; Avoid in psychotic patients
Nitrous oxide	Hypnosis Mild analgesia Anxiolysis	Erythrocytes	3-5 min	3-5 min	50-66% N_2O/O_2	Very short duration Inhalation agent	Often requires second agent to achieve adequate sedation; emesis; Requires special apparatus; Occupational exposure associated with spontaneous abortions
Dexmedetomidine*	Hypnosis Anxiolysis Some analgesia	Hepatic	2-5 min	~ 6 min	Load 1 mcg/kg/min over 5-10 minutes then 0.2-1 mcg/kg/hr infusion	Very short duration Preserves respiratory drive and airway reflexes Sedates patients who are insensitive to benzodiazepines	Expensive Bradycardia Hypotension
Etomidate*	Hypnosis Some amnesia	Hepatic	< 1 min	5-15 min	0.1-0.2 mg/kg over 1 minute	Very short duration; minimal cardiovascular effects	Airway obstruction and respiratory depression; myoclonus; emesis; adrenal suppression No analgesia
Propofol	Hypnosis Some amnesia	Hepatic	< 1 min	3-10 min	0.5-1.0 mg/kg over 1-2 minutes or 0.5 mg/kg titrated in 20 mg aliquots to desired effect.	Short acting Anti-emetic	Airway obstruction and respiratory depression; Hypotension (consider infusion rather than bolus); Pain at injection site; Allergy: soy and egg No analgesia
Methohexital*	Hypnosis Anxiolysis Amnesia	Hepatic	< 1 min	15 min	0.75-1 mg/kg IV bolus and can be redosed at 0.5 mg/kg every 3-5 minutes; 25 mg/kg rectal	Shorter acting, inexpensive, can be given rectally for pediatric sedation	Airway obstruction and respiratory depression; Hypotension and cardiovascular depression; Laryngospasm; No analgesia
Pentobarbital	Hypnosis Anxiolysis Amnesia	Hepatic	15-60 min	1-4 hours	Rectal:< 4 years: 3-6 mg/kg; >4 years: 1.5-3 mg/kg, max 100 mg; Adults 100 mg slow IV bolus; peds 2-5 mg/kg IV	Longer acting Multiple routes of administration	Airway obstruction and respiratory depression Prolonged duration Slow recovery associated with agitation No analgesia
*Off-label use for procedural sedation							

Medications (continued)

Drug	Effect	Elimination	Onset	Duration	Dosing	Pros	Cons
Midazolam	Hypnosis Anxiolysis Amnesia	Hepatic Active metabolite excreted renally	5-10 min (rectal); 3-5 min IV	1-4 hrs (rectal); 15-45 min IV; 1-2 hr IM	0.05-0.1 mg/kg IV (30-50% less in combo with opioid); Age greater than 70 years, half dose Age greater than 90 years, quarter dose	Reversal agent: flumazenil Shorter onset and duration than other benzodiazepines; Can be given intranasally	Airway obstruction and respiratory depression; Paradoxical excitement and disinhibition; Some hypotension; No analgesia
Alfentanil*	Amnesia Hypnosis at higher doses	Hepatic Active metabolite excreted renally	1 min	30-60 min IV	3-10 mcg/kg	Very short duration; less potent fentanyl; Reversal agent: naloxone	Minimal sedative effect; hypotension; hypoxemia; apnea; vomiting
Hydromorphone*		Hepatic	5-10 min	2-4 hrs IV	0.5-1 mg IV (Adult dose)	May work if patients are tolerant to morphine or fentanyl Reversal agent: naloxone	Histamine release
Morphine*		Hepatic Active metabolite excreted renally	5-10 min	2-4 hrs IV	4-8 mg (Adult dose)	Reversal agent: naloxone	Histamine release
Fentanyl*		Hepatic	1-2 min	30-60 min for single dose IV	0.5-1 mcg/kg every 1-2 min to effect	Less hypotension than other opiates; 100 times more potent than morphine; Reversal with naloxone	Minimal sedative effect; hypotension; hypoxemia; apnea; vomiting; chest rigidity when given fast
Flumazenil	Benzodiazepine receptor antagonist		1-2 min	30-60 min IV	0.1-0.5 mg		Rare agitation upon awakening Seizures, especially with chronic benzodiazepine users
Naloxone	Mu opioid receptor antagonist; reversal agent		1-2 min	20-40 min IV	0.04-0.5 mg		Hypertension Tachycardia Pain Diaphoresis
*Off-label use for procedural sedation							

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