Introduction to Procedural Sedation

Procedural sedation is common in emergency medicine. Proper sedation and analgesia improve the success of a procedure and increase satisfaction in patients and providers.[1] Prior to, and during painful procedures, one or more medications are administered to alleviate pain (analgesia), anxiety (anxiolysis), and/or provide dissociative sedation. Procedural sedation encompasses many topics (e.g., patient positioning, consent, equipment, etc.), however, the intent of this CAPSULES lesson is to focus on the pharmacology of commonly used medications during procedural sedation in the emergency department.

Is it Procedural Sedation?

A common misconception in the emergency department is that the selection of a certain medication defines procedural sedation. However, according to the latest guidelines,[1] "[t]he intent of the sedation, not necessarily the agent itself, determines whether medication is being delivered to relieve anxiety or facilitate a specific procedure..." This point is especially important with the increasing utilization of low-dose ketamine for analgesia in emergency departments.[2–7] Although ketamine is classified as a general anesthetic, administration of sub-dissociative doses to provide pain control does not constitute procedural sedation.

Levels of Sedation

Table 1 below summarizes the levels of sedation as defined in the 2014 American College of Emergency Physicians (ACEP) Clinical Policy on Procedural Sedation and Analgesia in the Emergency Department.[1]

	Minimal	**Moderate**	**Dissociative**	**Deep**	**General Anesthesia**
Alertness	Near baseline Normal response to verbal commands	Depression of consciousness Response to verbal or tactile commands	Trance-like cataleptic state Analgesia, sedation, amnesia	Depression of consciousness Difficult to arouse Respond to painful	No response to any stimuli Unarousable

	Minimal	Moderate	Dissociative	Deep	General Anesthesia
Ventilation / Cardiovascular	Unaffected	Unaffected	Unaffected	Ventilation often impaired	May be impaired
Example	Midazolam	Fentanyl + midazolam	Ketamine	Propofol	General Anesthesia

Table 1. Levels of Procedural Sedation

Patient Selection

For all patients scheduled to receive procedural sedation in the emergency department, a routine history should be obtained. The acronym 'AMPLE' may be used to obtain the most pertinent parts of the history.

A: Allergies
M: Current medications
P: Past medical history
L: Last meal for both liquids and solids

- Fasting states before procedural sedation have been a controversial topic in emergency medicine. One of the reasons for this is the extrapolation of guidelines from different clinical areas and professional societies.[1] At present, select institutions continue to follow the ASA guidelines, which state no solid food for 6 hours, liquids for 2 hours, and breast milk for 4 hours. However, the latest emergency medicine guidelines state:
  1. Procedural sedation should not be delayed (kids or adults) in the emergency department based on fasting times (Level B recommendation)
  2. Preprocedural fasting has not been shown to reduce the risk of aspiration or emesis during procedural sedation

E: Events causing the emergency department visit

- Special precautions should be taken in patients with trauma (e.g., cervical spine injury, intracranial injuries) and concomitant disease states (e.g., sepsis, seizure).

*In this CAPSULES lesson the dosing of all agents will be presented as mg/kg based on total body weight. Clinicians should be cautious when dosing obese patients. Certain agents may require

dosing based on ideal or adjusted body weight and careful titration until the desired effect is achieved.

Patient Monitoring

All patients should be monitored with pulse oximetry.

Intravenous access should be obtained in most patients.

During longer procedures patients should be positioned to minimize skin, musculoskeletal, or nerve damage.

Supplemental oxygen is commonly administered during procedural sedation. However, two studies examining supplemental oxygen during moderate sedation (propofol, and midazolam and fentanyl respectively)[8,9] found minimal to no benefit in prevention of hypoxemia.

Use of capnography during procedural sedation may detect hypoventilation earlier than pulse oximetry or clinical observation (Level B recommendation). Capnography may be especially useful in patients receiving supplemental oxygen, as desaturation may be delayed due to pre-oxygenation.[8,10,11] However, to date there is no data to support that the routine use of capnography reduces serious adverse outcomes in patients receiving procedural sedation (e.g., neurologic injury due to hypoxia, aspiration, or death).

There should be at least two persons during procedural sedation in the room. One qualified person (usually a nurse) for continuous monitoring of the patient and a provider credentialed in procedural sedation performing the procedure (Level C recommendation). In general practice, other personnel may be present to assist with patient positioning and other tasks that may arise.

Additional medications should be in the procedural room and quickly available if necessary. For example, medications that may be used during rapid sequence intubation, a code cart with necessary resuscitative equipment and medications, and reversal agents such as flumazenil or naloxone if indicated.

Selection of Pharmacologic Agents

When selecting the optimal medication for a procedure, the following should be considered: age of patient, level of sedation required (analgesia vs. anxiolysis, or both), and desired duration of sedation.

Certain institutions may have restrictions on anesthetic medications that can be ordered by emergency practitioners and personnel that may administer them.

Table 2 highlights the clinical characteristics of select medications commonly used for sedation and analgesia. Please see individual drug sections for more detailed information.

	Analgesia	Amnesia	Anxiolysis	Dissociation
Ketamine	X	X		X
Etomidate		X	X	
Propofol		X	X	
Methohexital		X	X	
Benzodiazepines		X	X	
Opioids	X			
Dexmedetomidine	X	X	X	
Ketamine/Propofol	X	X	X	X

Table 2: Pharmacologic agents and associated pharmacodynamic effects

Disposition

The majority of patients may be discharged home after undergoing procedural sedation in the emergency department. Rarely, procedural sedation patients may need to be admitted or observed in the hospital in cases of severe allergic reactions or concerning adverse effects. In general, patients should be awake, tolerating oral fluids, and have a safe way of traveling home. The return to normal mental status time frame varies with the selection of agent(s), dosing, and route of administration.[1]

Page References

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Ketamine

> **Grade:** Level A for kids, Level C for adults

Description

Ketamine is a general anesthetic agent commonly used for procedural sedation in the emergency department. Ketamine is a noncompetitive antagonist of NMDA (N-methyl D-aspartate) receptors in the central nervous system that blocks glutamate (an excitatory neurotransmitter). Ketamine increases atrioventricular conduction and has a direct depressant effect on the heart; however, hypotension and bradycardia are uncommon due to the release of endogenous catecholamines.[1] Centrally released catecholamines override the negative depressant effects of ketamine through increases in heart rate and blood pressure, while simultaneously providing bronchodilation through indirect beta-2 agonism in the lungs. Ketamine does not depress respiratory drive in response to carbon dioxide.[1]

The clinical effects of ketamine are dose- and patient-dependent. Low-dose ketamine (0.1-0.3 mg/kg) can provide analgesia,[2–7] while larger doses provide dissociative anesthesia. With dissociative dosing ketamine interferes with midbrain thalamic pathways blocking the cortex from sensory input.[8] During the dissociated state, patients preserve their respiratory drive, cardiac output, and do not respond to painful stimuli. Upper airway tone and protective airway reflexes remain intact. Nystagmus and "glazed eye stares" are common during disassociation. Ketamine also preserves and may increase skeletal muscle tone.[8]

Contraindications

The only labeled contraindications per the manufacturer are:[8]

- Patients in whom elevation of blood pressure would be a serious hazard
- Hypersensitivity to ketamine

Additional contraindications per ACEP guidelines:[9]

- Age < 3 months, due to increased risk of airway compromise
- Schizophrenia, as ketamine may exacerbate even when well controlled[10]

Relative contraindications per ACEP guidelines:[9]

- Procedures involving stimulation of posterior pharynx may increase laryngospasms (oropharyngeal procedures do not)
- History of airway instability
- Active pulmonary infection or disease
- Known or suspected cardiovascular disease (angina, heart failure, hypertension)
- Known central nervous mass, abnormalities, and hydrocephalus

- Porphyria or thyroid disorders

Common Ketamine Concerns

Increased intraocular pressure

The concern about increased intraocular pressure (IOP) from ketamine has existed since the 1960s. Increased IOP is thought to result from a combination of increased blood pressure and increased tension in extraocular muscles. However, controversy is evident even in early studies about the clinical significance of this increased IOP.[11,12] It is currently accepted that in a healthy eye, an increase of greater than 10 mmHg in IOP is clinically significant. For an injured eye, a 3-5 mmHg increase in IOP may be cause for clinical concern.[13]

A 2012 study examined 80 pediatric patients in the ED receiving ketamine for procedural sedation and found no increase in IOP in healthy eyes. However, baseline IOP was measured after ketamine induction.[14] In another pediatric study, 25 children with healthy eyes were found to have no increase in IOP; however, all participants received concomitant midazolam, glycopyrrolate, and ondansetron potentially confounding the effect of ketamine on IOP. The latest study in 2014[13] enrolled 60 kids between ages 8 to 18 with healthy eyes and found a median increase in IOP of 3 mm Hg, with fifteen patients having a transient increase ≥ 5 mmHg.

At present, the majority of emergency medicine literature on IOP from ketamine has been in the pediatric population. The data suggests no, or transient, increases in IOP with ketamine that are clinically insignificant. There is no data on the use of ketamine for patients seen in the ED that have glaucoma or acute globe injury, although 2011 ACEP guidelines list these conditions as relative contraindications to ketamine.

Increased intracranial pressure

Ketamine may indirectly increase mean arterial pressure. Historically, there has been concern about an increase in intracranial pressure (ICP) with ketamine. These concerns began with case reports in the late 1960s. Five case reports describe elevations in ICP that required additional interventions, such as drainage of cerebrospinal fluid (CSF) or hyperventilation. However, all cases had structural barriers to CSF flow (e.g., hydrocephalus).[15]

Although ketamine may transiently elevate ICP, there are numerous reports showing a decrease in ICP as well. Five systematic reviews were recently published on this topic analyzing over 1600 adult and pediatric patients (including critically ill, traumatic and nontraumatic brain injuries and illnesses). All concluded that there is no evidence of clinically significant changes in ICP from ketamine.[15–20]

Unless there is clear evidence of CSF obstruction, emergency clinicians should consider ketamine for procedures, rapid sequence intubation, and pain-relief in the critically ill and injured patients.[15]

Adult emergence phenomenon and adjunct benzodiazepines

One of the most common fears with ketamine, especially in the adult patient, is recovery agitation – commonly referred to as an emergence reaction. During recovery patients may experience disorientation and unpleasant hallucinations resulting in agitation. The reported incidence of emergence reactions varies between 0 to 30% in adults and 1.4 to 6.3% in children.[9]

Should prophylactic benzodiazepines be administered to adults? One double-blind placebo controlled trial in adults found that pretreatment with midazolam reduced the incidence of recovery agitation with a NNT of 6.[21] However, this study had many flaws including lack of classification of agitation reactions, clouding the true benefit of midazolam prophylaxis. Per the most recent guidelines, midazolam pretreatment is a "reasonable, but non-mandatory option."[9]

Should prophylactic benzodiazepines be administered to pediatric patients? Recovery agitation is much less common in children. One meta-analysis failed to show significant benefit from prophylactic benzodiazepines.[22] Current guidelines do not recommend prophylactic benzodiazepines in children.[9]

In order to minimize emergence, an attempt should be made to decrease external auditory, visual, and tactile stimulation during recovery, although the evidence for this is largely anecdotal. Adult patients and children (and their guardians) should be counseled about the effects of ketamine prior to the sedation. For severe agitation that is not responsive to redirection or other non-pharmacologic options, the recommendation is to administer a titratable dose of a benzodiazepine (e.g., midazolam 1 mg IV x 1-2 doses in an adult) as needed.[9]

To give or not to give: anti-emetics to prevent ketamine-associated nausea and vomiting?

Ketamine-associated vomiting in the recovery phase is common. The reported incidence of post-procedure vomiting with ketamine is 3.5 to 29.7%.[23] Vomiting may lead to dissatisfaction among the patient and emergency department staff, but is not a serious adverse event. The following have been correlated with increased nausea and vomiting with ketamine:[22,24,25]

- High initial intravenous dose ≥ 2.5 mg/kg
- Intramuscular route
- Adolescence (ages 9-14)
- Higher BMIs (≥ 25 kg/m2)

Few pediatric studies have analyzed the effect of prophylactic medications (there is no adult data to date). The risk of metoclopramide and atropine was questionable compared to the benefit.[26–28] Administration of oral ondansetron to children receiving intramuscular ketamine was ineffective in preventing emesis.[23] Intravenous ondansetron was shown to be effective in reducing emesis caused by intravenous ketamine in children, with a NNT of 13.[24]

Intravenous ondansetron is an inexpensive medication with little downside. It

ketamine sedation, especially in kids who may be at higher risk for nausea and vomiting and have intravenous access.

To give or not to give: anti-sialagogues to prevent airway compromise?

Ketamine may increase salivary and tracheobronchial secretions. There is concern that excess salivation may potentiate laryngospasm. Co-administration of atropine or glycopyrrolate can decrease airway secretions during a procedure and reduce post-procedure vomiting; however, there is no evidence that anti-sialagogues decrease or prevent stridor, laryngospasm, or apnea. The downsides of anti-sialagogues are tachycardia, a delayed onset of anti-sialagogue effect, side effects lasting longer than ketamine, increased agitation, and increased chance of a rash. Traditionally, the majority of emergency clinicians have omitted anti-sialagogues during procedural sedation,[1,26-28] and prophylactic atropine or glycopyrrolate are no longer recommended.[9]

Coronary artery disease

Ketamine is an indirect sympathomimetic that may cause increases in blood pressure, heart rate, cardiac output, and myocardial oxygen consumption.[1,9] Historically, there has been a concern about precipitating ischemia in older patients with significant coronary artery disease. However, ketamine has an excellent safety profile in all age groups, including during cardiac surgery in the elderly.[9] A recent study[29] measuring troponin levels after ketamine administration in 30 children found significant troponin elevations in two patients three hours after ketamine. None of the children had ECG evidence of ischemia or any cardiac sequelae. A large body of evidence supports the use of ketamine in all age groups. Nevertheless, caution should be exercised in patients who may be sensitive to sympathomimetics.

Administration and Dosage

In the emergency department ketamine may be administered intravenously, intramuscularly, and *intranasally for procedural sedation. Each route has different dosing ranges, advantages, and disadvantages[8,9] (Table 3).

	IV	IM
Recommended doses	1.5 – 2 mg/kg	4 – 5 mg/kg
Repeat dosing PRN	0.5 mg/kg	2 mg/kg
Onset	~1 min	~5 min
Duration	~10 – 15 min	~30 min
Pros & Cons	Fast Onset Shorter recovery Less emesis Rapid titration	Slower onset Longer recovery More emesis Difficult titration (repeat IM

IV	IM
emergency Preferred in adults	No IV securing (esp. in smaller kids) Preferred in kids and uncooperative patients

Rate of IV administration and laryngospasm, apnea, and respiratory depression

One large meta-analysis of over 8,000 ketamine procedural sedations found the incidence of laryngospasm to be 1 in 300. Large doses of IV ketamine were found to be an independent predictor of laryngospasm. The predictors for apnea were:[22]

- Large doses of IV ketamine
- Age > 12
- Addition of a prophylactic benzodiazepine

Rapid push administration of IV ketamine results in high central nervous system levels, and traditionally this has been thought to increase apnea and respiratory depression.[9] However, recent evidence with rapid push (< 5 seconds) administration of ketamine in children with forearm fractures did not report any laryngospasms, apnea, or depression in respiratory drive.[30] However, this study did use lower doses of ketamine (< 1 mg/kg).

The recommendation per manufacturer[8] is to administer bolus doses of ketamine no faster than 60 seconds, and this may be the safest practice until trials with full dosing of ketamine confirm the safety of more rapid administration.

Intranasal administration

There is increased interest in intranasal administration of ketamine in the emergency department. Most studies have focused on analgesic properties of ketamine when administered intranasally.[31] Pharmacokinetically, much larger doses are needed to achieve dissociation when ketamine is administered intranasally (~10 mg/kg).[31,32] The volume needed for intranasal administration usually limits such large doses. For example, a 30 kg child will need ~300 mg of ketamine or 3-6 mls instilled intranasally (depending on ketamine concentration 50 mg/ml or 100 mg/ml). In an irritated, crying child large volume intranasal administration may not be feasible and traditional IV or IM routes are more advantageous.

Page References

Quizzes	Status
Ketamine Quiz	

PREVIOUS LESSON

Ketamine Quiz

A 7 year old boy is presenting to a moderately busy emergency department with a distal radial/ulnar fracture after falling off his skateboard. His past medical history includes seizures that are well controlled on levetiracetam. His last meal was 4 hours prior to presentation and he drank a half-glass of orange juice while in triage. His pain has been poorly controlled with intranasal fentanyl while obtaining x-rays. The orthopedic consult physician is bedside immediately and ready to begin the reduction and casting pending procedural sedation.

Question 1 of 5

1 point(s)

According the latest ACEP guidelines, procedural sedation for this patient should:

- ○ Be delayed for 6 hours
- ○ Be delayed for an additional 2 hours
- ○ Not be delayed based on last oral intake
- ○ Be delayed for 4 hours

CHECK

Ketamine Quiz

A 7 year old boy is presenting to a moderately busy emergency department with a distal radial/ulnar fracture after falling off his skateboard. His past medical history includes seizures that are well controlled on levetiracetam. His last meal was 4 hours prior to presentation and he drank a half-glass of orange juice while in triage. His pain has been poorly controlled with intranasal fentanyl while obtaining x-rays. The orthopedic consult physician is bedside immediately and ready to begin the reduction and casting pending procedural sedation.

Question 1 of 5

1 point(s)

According the latest ACEP guidelines, procedural sedation for this patient should:

- ○ Be delayed for 6 hours
- ○ Be delayed for an additional 2 hours
- ◉ Not be delayed based on last oral intake
- ○ Be delayed for 4 hours

Correct

According to the most recent procedural sedation guidelines by ACEP, preprocedural fasting has not been shown to reduce the risk of aspiration or emesis during procedural sedation. Procedural sedation should not be delayed (kids or adults) in the emergency department based on fasting times (Level B recommendation).

Ketamine Quiz

A 7 year old boy is presenting to a moderately busy emergency department with a distal radial/ulnar fracture after falling off his skateboard. His past medical history includes seizures that are well controlled on levetiracetam. His last meal was 4 hours prior to presentation and he drank a half-glass of orange juice while in triage. His pain has been poorly controlled with intranasal fentanyl while obtaining x-rays. The orthopedic consult physician is bedside immediately and ready to begin the reduction and casting pending procedural sedation.

Question 2 of 5

1 point(s)

Ketamine should not be used for procedural sedation as it is contraindicated in patients with a history of seizures.

- ◉ False
- ○ True

Correct

Seizure is not a relative or absolute contraindication for ketamine.

NEXT

Ketamine Quiz

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Question 3 of 5

1 point(s)

Despite contraindications you decide to administer ketamine. The ideal route of administration for our patient is:

- ○ Intranasal
- ○ Intramuscular
- ◉ Intravenous
- ○ Rectal

Correct

Intravenous route is most ideal. Older kids are generally more directable and starting intravenous access prior to the procedure is usually possible. A radial/ulnar fracture reduction and casting is a painful procedure and having an intravenous access for repeat ketamine dosing is convenient. In case of an emergency an IV line would be present. Shorter recovery time and less

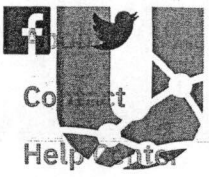
administration. Intranasal administration would require large volumes of ketamine to be instilled into the nares while rectal administration for procedural sedation in the ED has not been studied.

NEXT

Join the discussion

Commenting as **Stephanie Dabulis**

POST COMMENT



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Ketamine Quiz

A 7 year old boy is presenting to a moderately busy emergency department with a distal radial/ulnar fracture after falling off his skateboard. His past medical history includes seizures that are well controlled on levetiracetam. His last meal was 4 hours prior to presentation and he drank a half-glass of orange juice while in triage. His pain has been poorly controlled with intranasal fentanyl while obtaining x-rays. The orthopedic consult physician is bedside immediately and ready to begin the reduction and casting pending procedural sedation.

Question 4 of 5

1 point(s)

You opt to administer a prophylactic dose of intravenous ondansetron prior to ketamine administration. According to this CAPSULE lesson, how many patients need to be treated to prevent one emesis?

- ○ ~1 in 100
- ○ ~1 in 50
- ◉ ~1 in 10
- ○ ~1 in 1000

Correct

The best evidence to date shows that a one-time intravenous dose of ondansetron prior to intravenous ketamine reduces post procedural emesis (NNT=13).

Ketamine Quiz

A 7 year old boy is presenting to a moderately busy emergency department with a distal radial/ulnar fracture after falling off his skateboard. His past medical history includes seizures that are well controlled on levetiracetam. His last meal was 4 hours prior to presentation and he drank a half-glass of orange juice while in triage. His pain has been poorly controlled with intranasal fentanyl while obtaining x-rays. The orthopedic consult physician is bedside immediately and ready to begin the reduction and casting pending procedural sedation.

Question 5 of 5

1 point(s)

All of the following are possible predictors of laryngospasm and apnea with ketamine, except:

- ○ Prophylactic benzodiazepines
- ◉ Prophylactic glycopyrrolate or atropine
- ○ Age > 12
- ○ Large ketamine doses

Correct

The best evidence to date shows the following predictors for laryngospasm and apnea with ketamine: age >12, large doses of IV ketamine, and addition of prophylactic benzodiazepines. Laryngospasm with ketamine remains a significant but rare event that is usually responsive to supportive care (bag-valve mask support).

Propofol

> **Grade:** Level A recommendation for kids and adults

Description

Propofol is another commonly used general anesthetic for procedural sedation in emergency medicine. Propofol is thought to work as an agonist at $GABA_A$ receptors and as an antagonist at NMDA receptors. Propofol rapidly distributes after intravenous bolus administration resulting in rapid sedation that is proportional to the dose administered. Propofol may be used for moderate or deep sedation (as defined by Joint Commission).[1] The rapid onset, titratability, short duration of action, quick recovery, antiemetic, antiepileptic, and antipruritic properties of propofol make it an ideal anesthetic agent in emergency medicine.[2–4] As propofol does not possess analgesic properties, concomitant analgesics may be needed for painful procedures. Propofol remains one of the most studied procedural sedation agents with multiple studies confirming safety and efficacy in over 26,000 patients in the emergency department setting, earning a level A recommendation from ACEP for both kids and adults.[4]

As propofol is highly hydrophobic it is suspended in a fat emulsion containing soybean oil, egg lecithin, and glycerol. It is this lipid emulsion that that gives propofol its distinct milky-white appearance. The presence of triglycerides in propofol is rarely an issue for patients given limited doses of propofol for procedural sedation. However, triglycerides may accumulate in patients

Further, as propofol is an emulsion, the stock vial should be shaken well before drug aspiration and administration.[3]

Propofol may decrease arterial blood pressure. The hypotensive effects of propofol are especially pronounced in patients with impaired left ventricular function, dehydration, and the elderly. Standard induction doses of propofol (1-2 mg/kg) can frequently cause apnea lasting 30-60 seconds.[2]

Contraindications

- Allergy to propofol
- Allergy to eggs, egg products, soybeans, or soy products

Common Propofol Concerns

Propofol pain on injection and the use of lidocaine

Propofol may cause vein irritation upon administration. Local pain is especially pronounced if small veins on the hand are used for injection (45% of children experienced injection pain when a small vein on the hand was used). Further, 70% of postoperative patients in one systematic review recalled pain upon injection of propofol.[5]

In order to minimize propofol injection pain, large antecubital veins are preferred. When antecubital veins are utilized <10% of patients report injection site pain. Injectable lidocaine may be used to minimize injection pain; however, in our practice, we do not routinely use lidocaine with propofol.[3]

Apnea

Propofol's most concerning risk during procedures is apnea. In one prospective observational study in Australia, administration of propofol to 400 patients resulted in 86 (22%) respiratory adverse events that led to 123 respiratory interventions. The interventions consisted of: basic airway maneuvers (27.8%), bag-valve-mask support (2.3%), and suctioning (0.8%). None of the patients experienced aspiration, endotracheal intubation, or laryngeal mask insertions.[6] In another Dutch emergency department study of 386 adult and pediatric patients receiving 1 mg/kg of propofol as an induction dose, the following were reported: hypoventilation 42 (11%), desaturation 19 (5%), hypotension 11 (3%), and bradycardia 3 (1%). There were no aspirations or endotracheal intubations documented, and all respiratory adverse events resolved with basic airway maneuvers.[7] The overall reported incidence of ED propofol-associated apnea in both children and adults ranges between 4.8% to 31%, with highest incidence seen in patients without preprocedural supplemental oxygen. In these same studies the desaturations necessitated bag-valve-mask support in 0% to 4.6% of patients.[1]

Transient apnea from propofol is not uncommon. However, most studies in the emergency department setting report resolution with basic airway maneuvers. The use of capnography during procedural sedation with propofol may alert emergency clinicians earlier to apnea than pulse oximetry alone.[8–10] Emergency clinicians should consider using smaller initial doses or longer periods between titration doses to minimize the risk of apnea. This strategy is especially important in the elderly or debilitated patients (ASA score III or IV), or in patients pretreated with opioids, as such patients are at an increased risk of respiratory adverse events with propofol.[1–3]

Hypotension

Patients that may be dehydrated or have blood loss are more sensitive to the hypotensive effects of propofol. If a patient's underlying condition and time permit, volume should be optimized before administration of propofol.[1] In one study of more than 700 patients receiving propofol for procedural sedation, a transient drop in blood pressure (>20%) occurred in 3.5% of cases without any long-term sequelae.[11]

Propofol Related Infusion Syndrome[12]

Propofol-related infusion syndrome (PRIS) is a constellation of metabolic derangements that have been associated with propofol infusions. PRIS results in severe metabolic acidosis, kidney and liver dysfunction, rhabdomyolysis, and bradycardia and cardiovascular collapse. Known risk factors for PRIS include:

- High-dose propofol infusions (> 60 mcg/kg/min)
- Prolonged infusions (> 48 hours)
- Young age
- Critical illness with corticosteroid and pressor support
- Inborn errors in mitochondrial metabolism

Short intravenous boluses for procedural sedation in the ED have not been reported to cause PRIS.

Propofol dosage and administration

Recommended dosing:	1 mg/kg bolus

Propofol dosage and administration

Repeat PRN doses:	0.5 mg/kg every 3 minutes
Onset:	Immediate
Duration:	~5 – 15 minutes

* When given as a 1 mg/kg bolus, followed by 0.5 mg/kg until sedation is achieved, amnesia persists for about 15 minutes[13]

The recommended dosing is based on total body weight for younger patients (<55 years of age) without significant comorbidities. Dose and administration rates should be reduced in older or frail patients.[1]

Concomitant analgesia

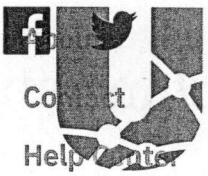
Propofol does not provide analgesia. Traditionally, there are two approaches in administering analgesia for painful procedures in the ED:

1. Patient's pain is well controlled with opioid analgesics before the start of the procedure. Patients are given only propofol for the procedure. (e.g., shoulder reduction)
2. An opioid, usually fentanyl, is administered immediately prior to the administration of propofol. (e.g, cardioversion)

There are a few considerations with co-administration of analgesic medications. Pain is a powerful respiratory stimulus. Once pain is eliminated with the procedure (e.g., reduction) patients may become more sensitive to the synergistic effects of opioids and propofol. Furthermore, immediate co-administration of opioids with propofol increases the risk of adverse events.[10]

little prn BDZ take 3mg/kg to get sleepy. Propofol can be tough in general, so I just go in and prepare my team for anything and also make sure we are treating pain first. I have not come across any literature that compares the different sedatives in the ED substance abuse population, however I'm sure there is something in the anesthesiology lit. Anecdotally, I find ketamine to be much more consistent as far as dose/response...if you dose it right.

Reply



Propofol Quiz

A 28 year old man is presenting to the emergency department with a dislocated shoulder after a mixed-martial arts class. His past medical history is noncontributory except occasional shoulder dislocations for which he states "it's been a while, but I usually need to be knocked out to fix." There is no neurovascular injury concern and a portable x-ray reveals an anterior dislocation without any evidence of fracture. His pain is 10/10 and scapular manipulation, external rotation, and Stimson technique have failed. Your plan is for procedural sedation with propofol and shoulder traction/countertraction.

Question 1 of 4

1 point(s)

According to the latest ACEP guidelines, which level of sedation is likely to occur?

- ○ Moderate
- ◉ Deep
- ○ Minimal
- ○ General anesthesia

Correct

Patient is in extreme pain and minimal or moderate sedation are likely to be unsuccessful. General anesthesia is not warranted for a simple shoulder reduction. An adequate dose of propofol for this reduction is likely to result in deep sedation.

Propofol Quiz

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Question 2 of 4

1 point(s)

All of the following are contraindications to propofol, except:

- ○ Allergy to egg
- ○ Allergy to soy
- ○ Allergy to propofol
- ◉ Allergy to milk

Correct

Propofol is highly hydrophobic drug suspended in a fat emulsion containing soybean oil, egg lecithin, and glycerol. An allergy to any of these components contraindicates the use of propofol.

NEXT

Propofol Quiz

A 28 year old man is presenting to the emergency department with a dislocated shoulder after a mixed-martial arts class. His past medical history is noncontributory except occasional shoulder dislocations for which he states "it's been a while, but I usually need to be knocked out to fix." There is no neurovascular injury concern and a portable x-ray reveals an anterior dislocation without any evidence of fracture. His pain is 10/10 and scapular manipulation, external rotation, and Stimson technique have failed. Your plan is for procedural sedation with propofol and shoulder traction/countertraction.

Question 3 of 4

1 point(s)

Our patient has not received any analgesia since his arrival to the emergency department. Which of the following regarding the timing of analgesia is most correct?

- ○ Opioids should not be administered as patient is scheduled for procedural sedation.
- ◉ Opioids should be given now and pain well controlled. If the patient has adequate analgesia there is no need for prophylactic opioids immediately prior to propofol.
- ○ Opioids should be given now, and prophylactically immediately before the start of the procedure.
- ○ Opioids should only be given once the shoulder is reduced and there is ongoing pain.

Not providing analgesia to a patient with 10/10 pain from trauma is poor care. Administering opioids immediately prior to propofol may be reasonable in certain procedures but this practice may increase the risk of respiratory adverse events. The latest clinical policy advisory on administration of propofol in the emergency department recommends controlling the pain with opioids before the start of the procedure and, if possible, avoiding concomitant administration of opioids with propofol.

NEXT

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Commenting as **Stephanie Dabulis**

POST COMMENT

Rahma Salim October 13, 2017 at 6:47 am

concise and helpful for clinical practice.

Reply

Propofol Quiz

A 28 year old man is presenting to the emergency department with a dislocated shoulder after a mixed-martial arts class. His past medical history is noncontributory except occasional shoulder dislocations for which he states "it's been a while, but I usually need to be knocked out to fix." There is no neurovascular injury concern and a portable x-ray reveals an anterior dislocation without any evidence of fracture. His pain is 10/10 and scapular manipulation, external rotation, and Stimson technique have failed. Your plan is for procedural sedation with propofol and shoulder traction/countertraction.

Question 4 of 4

1 point(s)

Our patient has asked us about possible adverse effects of propofol. What should we tell him? (choose all that apply)

- ☑ This drug may decrease your blood pressure and we may have to give you a bolus of fluids
- ☑ Drug may hurt when injected into the vein
- ☑ This drug may cause you to stop breathing and we may have to temporarily breathe for you

Correct

Propofol's adverse effects include pain upon injection, apnea, and hypotension and bradycardia.

Ketofol (combination of ketamine and propofol)

Description

The combination of ketamine and propofol for the purposes of procedural sedation in the emergency department has grown in popularity in recent years. There are a number of theoretical benefits associated with this practice. These include:[1–3]

- Combination of ketamine and propofol may mitigate each agent's respective adverse effects:
  - Hypotension secondary to propofol may be balanced by the sympathomimetic effects of ketamine
  - Ketamine is associated with vomiting, whereas propofol has antiemetic properties
  - Respiratory depression seen with propofol may be potentially reduced when combined with ketamine due to a lower overall dose of propofol administered
  - Propofol possesses no analgesic properties whereas ketamine does
- Shorter recovery time than ketamine alone
- When used in combination, the doses of each are reduced due to synergy

There is limited evidence that procedural sedation is smoother and more predictable with ketofol than with propofol alone.[4–10] In a prospective case series of 219 children, the combination of ketamine and propofol resulted in median recovery time of 14 minutes.[6] However, in a blinded randomized trial of 136 children requiring procedural sedation secondary to orthopedic injury, total sedation time was only three minutes shorter with ketofol relative to ketamine with less vomiting and higher patient and provider satisfaction scores with the combination of agents.[4] A recently published systematic review and meta analysis of ketamine-propofol combination versus propofol alone for procedural sedation in the emergency department demonstrated no significant differences related to overall adverse events, sedation time, procedure time, and recovery time, but did show fewer adverse events related to respiratory depression with the ketofol combination versus propofol alone.[11]

Dosage, Administration, and Preparation

Various admixtures of ketofol have been evaluated, ranging from 1:1 to 1:4 admixtures of ketamine and propofol.[12,13] One proposed method is described below:

Two Drugs in One Syringe (1:1 Admixture)

1. Combine 5 ml of ketamine 10 mg/mL + 5 ml of propofol 10 mg/mL in a 10 ml syringe
2. The resulting concentration is 5 mg/mL for each drug
3. Administer 0.1 mL/kg = 0.5 mg/kg IV of each drug in aliquots titrated to effect

It is important to note that physical admixture of the medications within the same syringe requires proper labeling with denotation of the exact concentration and amount of ketamine and propofol contained within the syringe.

However, propofol is more short-acting relative to ketamine. *Giving the above admixture*

Independent administration of both agents has been advocated,[14] as repeated boluses of ketamine and propofol combined in the same syringe may lead to longer recovery time due to larger doses of ketamine.

An alternative (preferred) method of administering both agents during procedural sedation is as follows:

Two Drugs in Two Syringes

1. Administer ketamine 0.5 mg/kg IV bolus first, then
2. Administer propofol 1 mg/kg IV bolus
3. Repeat additional boluses of only propofol 0.2 – 0.5 mg/kg IV as needed

Common Ketofol Concerns

In studies evaluating the combination of ketamine and propofol, hypotension occurs less frequently than with propofol alone. However, propofol-induced hypotension is typically transient and responsive to fluids.

Few differences in respiratory depression have been demonstrated despite the belief that ketofol results in less respiratory depression than propofol alone. Lower doses of propofol may be used with ketofol which may reduce the risk of respiratory adverse events.

Ketofol may result in less recovery agitation than ketamine alone, particularly for adults. In addition, ketofol may result in less vomiting than ketamine alone; however, reduction of vomiting with ketamine can also be achieved by prophylactic administration of ondansetron.[4–10]

Lastly, ketofol entails the administration of multiple agents. The modest benefits of a shorter recovery time should be balanced with additional time needed for medication preparation, calculations, double-checks, and an increased risk of medication errors.

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Ketofol Quiz

Question 1 of 1

1 point(s)

Which of the following is *not* part of the rationale for combining the use of ketamine and propofol (ketofol) for procedural sedation?

- ○ Mitigation of adverse events associated with either agent
- ○ Shorter time to recovery with ketofol following procedural sedation
- ○ Lower doses of either agent utilized due to synergy
- ◉ Current evidence suggests a smoother and more predictable procedural sedation with ketofol

Correct

At this time, there is inadequate scientific evidence to suggest that ketofol allows for a predictable duration and length of procedural sedation relative to the use of either agent alone. If ketamine and propofol are used together, monitoring should be considered and conducted similarly as with the use of either agent alone.

FINISH QUIZ

Etomidate

> **Grade:** Level C for kids, Level B for adults

Description

Etomidate is the most commonly used induction agent for rapid sequence intubation in the emergency department. Etomidate is well liked by emergency clinicians due to its quick onset of action and brief duration, but most importantly due to minimal effects on heart rate, stroke volume, ventricular filling pressures, and myocardial oxygen consumption.[1–6]

Transient desaturation occurs in ~10% of patients receiving etomidate for procedural sedation.[7] Other disadvantages of etomidate include myoclonus and adrenal suppression,[8] both which will be discussed further below.

Contraindications

Allergy to etomidate

Common Etomidate Concerns

Myoclonus

myoclonus resulting from etomidate in the emergency department is masked

succession. however, between 20% to 45% of patients receiving etomidate for procedural sedation exhibit myoclonus, spontaneous muscle movement, or increased muscle tone.[7,9–11] these adverse effects may not be desirable during procedures where a flaccid state is desired. the incidence of myoclonus may be decreased by pretreatment with opioids or benzodiazepines;[1] however, this can result in increased adverse events and a prolonged recovery time.

electroencephalogram studies have shown that myoclonic movements during sedation with etomidate are not related to seizures.[11] however, etomidate has been used as a diagnostic agent to induce seizure foci and can precipitate a seizure in patients with epilepsy.[1] although seizure history is not an absolute contraindication to etomidate, other agents such as propofol or ketamine may be a safer option in patients with epilepsy.

Adrenal Suppression

the concern for etomidate's effect on adrenal suppression began in the 1980s with several studies showing a decrease in cortisol levels shortly after administration.[12,13] This was followed by decades of studies showing worse outcomes in critically ill patients,[14–16] and other studies showing no deleterious effect on patient-specific outcomes.[10,17–20] Perhaps the strongest evidence to date comes from two studies:

1. An analysis of over 700,000 ICU patients showing that one-time doses of etomidate as an induction agent for intubation were not associated with increased mortality or other patient-oriented adverse clinical outcomes.[18]
2. A Cochrane meta-analysis showing no evidence that one-time doses of etomidate increase mortality or healthcare resource utilization in critically ill patients.[21]

To date the use of etomidate for procedural sedation and the effect on adrenal suppression has not been studied. A large body of safety data from critically ill patients supports the use of etomidate in otherwise healthy patients.

Dosage and Administration

Etomidate dosage and administration

Recommended dosing:[11]	0.1 – 0.2 mg/kg IV bolus
Repeat PRN doses:	0.05 mg/kg every 3 – 5 minutes
Onset:	~60 seconds
Duration:	~3 – 5 minutes

Etomidate pain on injection

Etomidate is a highly irritating solution and may cause significant pain and burning upon administration in up to 40% of patients.[7,11] To decrease etomidate's pain upon injection, similar steps may be taken as with propofol administration (use of larger antecubital veins or pretreatment with a small amount of injectable lidocaine). Patients who report severe burning upon injection of etomidate are more likely to experience myoclonus during the procedure. In non-emergent situations etomidate should be administered over 60 seconds.[11]

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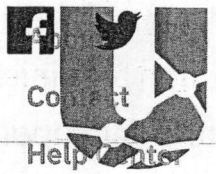

Etomidate Quiz

Question 1 of 1

1 point(s)

All of the following are true regarding etomidate during procedural sedation, except:

- ○ It may cause myoclonus in a significant proportion of patients
- ○ During injection patients may experience a burning sensation in the vein
- ◉ The usual procedural sedation doses will cause clinically significant adrenal suppression
- ○ Etomidate may not be the best agent for procedures where a motionless state is desired

Correct

Myoclonus occurs between 20% and 45% of patients receiving etomidate. As myoclonus is common, etomidate may not be the best option for patients where a relaxed or motionless state is needed for the procedure. Etomidate may cause burning upon injection in up to 40% of patients. To date there is no data on adrenal suppression in patients receiving etomidate for procedural sedation. However, even in critically ill patients, one dose of etomidate does not result in clinically significant adverse outcomes.

FINISH QUIZ

Methohexital

Description

Methohexital is an ultra-short acting oxy-barbiturate that may be used for brief procedures. The advantage of methohexital is its immediate onset and short duration of action. Methohexital is approximately three times as potent as thiopental with an induction dose lasting approximately 5 minutes.[1] The U.S. brand name Brevital® is derived from brevis, Latin for "short," reflecting its rapid onset and clearance of the drug when administered intravenously. As with ketamine, methohexital may be given intramuscularly. Methohexital may also be administered rectally for pediatric procedures.[2–4] Methohexital does not have analgesic properties.[2]

Methohexital, like all barbiturates, can decrease cardiac output and blood pressure while increasing heart rate. This occurs due to venodilation and activation of the baroreceptor reflex that usually maintains hemodynamic stability during procedural sedation. Although methohexital induction doses do not depress laryngeal reflexes, as with propofol, apnea is a common adverse event.[1,2] Much like propofol, methohexital is a potent anticonvulsant and is effective in reducing intracranial pressure.[1]

With the introduction of generally safer options like propofol and ketamine, methohexital has become a less popular option for procedural sedation in emergency medicine. However, with recent drug shortages (e.g., propofol) emergency clinicians should remain familiar with methohexital, an anesthetic with a 75-year track record.[1]

Contraindications

- Allergy to barbiturates or methohexital
- Porphyria
- BLACK BOX WARNING[2]
  - Methohexital is the only procedural sedation agent with a boxed warning. In short, the warning states that methohexital needs to be administered in settings where continuous monitoring of cardiorespiratory function is available. The label also warns about the need of a provider skilled in airway management to be present. Finally, the clinician performing the procedure should not be the same individual monitoring the patient.

Common Methohexital Concerns

Apnea

Methohexital may decrease respiratory drive or cause apnea with the usual doses used during procedural sedation.[2,4–10] In one emergency department study comparing intravenous methohexital and propofol for fracture/dislocation reductions, transient respiratory depression occurred in 48% and 49% of cases, respectively.[6] In another retrospective emergency department study, desaturation/hypoventilation occurred in 14% of patients receiving intravenous methohexital.[7] A case series in a pediatric emergency department resulted in 5.5% cases with transient hypoventilation after intravenous methohexital.[8] In another prospective descriptive pediatric study of rectal methohexital in children undergoing CT scans, 6% of patients had transient oxygen desaturations.[4] All of the reported desaturations in the emergency department studies and resolved with basic airway maneuvers

(repositioning and bag valve mask support) and no patients required intubation.

The largest study to date on methohexital's adverse events comes from a database of oral and maxillofacial surgeries.[5] The study included over 47,000 patients receiving sedation in the outpatient setting with 55% receiving propofol, 33% methohexital, and 12% benzodiazepines. Compared to propofol, methohexital resulted in higher incidence of laryngospasm (0.4 vs 0.02%) and hypoventilation (0.07 vs. 0.02%). The authors concluded that propofol resulted in the lowest risk of adverse events when compared to methohexital or benzodiazepines.

Dosage and Administration

	IV	IM	PR
Recommended doses[2,11]	0.5-1 mg/kg	5-10 mg/kg	25 mg/kg
Repeat dosing PRN	0.5 mg/kg every 2-5 minutes	n/a	n/a
Maximum Dose	2 mg/kg	n/a	500 mg
Onset	Immediate	2-10 minutes	5-15 minutes
Duration	< 10 minutes	10-20 minutes	45 minutes

	IV	IM	PR
Concentration to be used	1% (10 mg/ml)		1% or 10% (10 mg/ml or 100 mg/ml)
Pros & Cons	Rapid onset Easy titration	Not recommended in adults Less predictable	Not recommended in adults 17% absorbed from rectum Longer duration (useful for pediatric imaging)

Routes

The emergency department studies discussed in this section describe the use of the rectal route in pediatric patients, and the intravenous route in children and adults. However, per the manufacturer, the intravenous administration of methohexital is only approved in adults, while intramuscular and rectal administration in children only. Further, neonates (< 1 month of age) should not receive methohexital.[2]

Drug preparation

Methohexital needs to be reconstituted at the bedside due to the short stability of the drug. Confusion with bedside dilutions is common and

can lead to error. The following describes how to dilute a 500 mg stock vial of methohexital to achieve the desired concentration.[2]

- Methohexital 500 mg vial is diluted with 50 ml of sterile water for injection for a 1% or 10 mg/ml solution for IV injection or rectal administration.
- Methohexital 500 mg vial is diluted with 10 ml of sterile water for injection for a 5 % or 50 mg/ml solution for IM injection only.
- Methohexital 500 mg vial is diluted with 5 ml of sterile water for injection for a 10% or 100 mg/ml solution for rectal administration only.

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PREVIOUS LESSON

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Fentanyl and Midazolam

Fentanyl

Description

As an opioid analgesic, fentanyl is rarely used as a sole agent for procedural sedation. Fentanyl is primarily used in combination with sedative-hypnotics such as midazolam for the purposes of moderate sedation or etomidate and propofol for deep sedation.

Fentanyl acts as an agonist of opioid receptors distributed throughout both the peripheral and central nervous systems. It is a synthetic analog of meperidine, and it is considered to be 100 times more potent than morphine. As a result of its high lipid solubility, fentanyl is able to rapidly cross the blood-brain barrier to produce its analgesic effects. Fentanyl has a relatively quick onset of action, generally resulting in analgesia within two to three minutes following intravenous administration, and its duration of action is between 20 and 30 minutes. It is completely metabolized by the liver to inactive metabolites, allowing for its use in the setting of renal and hepatic dysfunction, and its estimated serum half-life is 90 minutes. With these properties, fentanyl is an agent that can easily be titrated upward to produce analgesia, but bearing in mind that as a result of its high lipid solubility it may accumulate in the adipose tissue, leading to a prolonged analgesic effect.[1,2]

Common Fentanyl Concerns

Respiratory depression is one major concern with co-administration of fentanyl and midazolam (or propofol). Fentanyl not only interacts with the respiratory center within the brainstem to produce a decrease in ventilatory drive through decreased sensitivity to hypoxia and hypercarbia, but it also has an effect in the pons and medulla where respiratory centers are involved in the regulatory rhythm of breathing, leading to a decrease in respiratory rate and tidal volume in a dose-dependent fashion.[3,4] Another factor that may be associated with respiratory depression and apnea includes the rapid rate of administration of intravenous fentanyl. It is important to note that the duration of respiratory depression may be longer than the analgesic effect induced by fentanyl.

One unique phenomenon associated with rapid administration of intravenous fentanyl is chest wall rigidity. This has been demonstrated at doses of fentanyl that exceed 5 mcg/kg, and has been shown to occur more commonly in the pediatric population. It is hypothesized that this effect occurs as a result of the binding of fentanyl to the mu and kappa receptors at the spinal cord and basal ganglia, which is controlled through the gamma-aminobutyric acid (GABA) pathways at these sites.[5,6] Although naloxone has reversed this effect in some case reports, it may not lead to complete antagonism of this phenomenon and its onset of action may be up to one minute; laryngospasm may occur as a result, necessitating neuromuscular paralysis and emergent intubation. Chest wall rigidity can be avoided by administering intravenous fentanyl over a period of three to five minutes followed by adequate flushing of the intravenous line tubing in a slow and cautious manner.

Unlike other opioid analgesics, fentanyl alone rarely causes bradycardia and hypotension, as it is not associated with histamine release, making it an optimal agent in the setting of hemodynamic instability.[7]

Administration and Dosage

For the purpose of procedural sedation, the initial dose of intravenous fentanyl ranges between 1 and 2 mcg/kg (usually 50 to 100 mcg), which is administered prior to the sedative agent of choice. Once fentanyl and the sedative are administered, clinicians can titrate either agent upward to the desired level of sedation or analgesia as deemed necessary.[8]

Fentanyl may be administered intranasally, especially in pediatric patients and in those patients where intravenous access may be difficult to obtain. With this route of administration, dosing of fentanyl typically remains the same as the intravenous route (1 to 2 mcg/kg) for procedural sedation, but for total doses that exceed 1 mL (when utilizing formulations of concentrations of 50 mcg/mL), one-half of the dose should be administered in each nostril.[9]

Midazolam

Description

Midazolam is a short-acting benzodiazepine with sedative-hypnotic properties and potent amnestic effects. It is effective when used as a sole agent for procedural sedation. However, as midazolam does not possess analgesic properties, it is often co-administered with an analgesic to produce a synergistic effect during procedural sedation.

Midazolam binds to the benzodiazepine receptor sites within the GABA system, thereby increasing the activity and strength of the interaction between GABA and its GABA receptors, which leads to an increase in the chloride current through the chloride channel. As a water-soluble agent, midazolam provides optimal pharmacokinetic properties for the purposes of procedural sedation. Following intravenous administration, midazolam has an onset of action of 1 to 2 minutes and a duration of action between 30 and 60 minutes, allowing for ease of titration.[8,10]

Common Midazolam Concerns

Midazolam is associated with hemodynamic and respiratory adverse effects, which typically occurs in a dose-dependent manner. The risk of hypotension as well as hypoventilation, hypoxia, and apnea may be increased in the elderly and with co-administration of other central nervous system depressants.[3,4,8]

Another adverse event associated with midazolam (and other benzodiazepines) is paradoxical excitation and agitation, which can occur in up to 15% of all patients who undergo procedural sedation. If this occurs, flumazenil should be readily available at the bedside for reversal of this phenomenon.[8,10]

Administration and Dosage

Route	Initial Dose	Notes
Oral	0.5 mg/kg	Onset within 30 minutes Not preferred route for procedural

Route	Initial Dose	Notes
		sedation due unreliable sedation secondary to first-pass metabolism
Intravenous	0.025 – 0.1 mg/kg	Most predictable pharmacokinetic properties Titrate upward slowly to effect every 3 to 5 minutes
Intramuscular	0.025 – 0.1 mg/kg	Not preferred route for procedural sedation in adults due to erratic and unpredictable pharmacokinetic properties
Intranasal	0.2 mg/kg	Onset within 15 minutes For total doses that exceed 1 mL, one-half of the dose should be administered in each nostril Generally found to be irritating to the nasal mucosa and not well-tolerated by crying and agitated children

Fentanyl and Midazolam Final Word

The combination of fentanyl and midazolam for procedural sedation has become less popular with the introduction of propofol and ketamine. Although easily titratable, the longer half-lives of fentanyl and midazolam may prolong recovery time in and out of the emergency department. The

effect resulting in an increased risk of apnea and respiratory depression, especially during painful procedures requiring a deeper level of sedation. If used, the combination of fentanyl and midazolam is best suited for minor procedures needing minor to moderate sedation. For deeper levels of sedation other agents are recommended.[11]

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Fentanyl and Midazolam

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Fentanyl and Midazolam

Question 1 of 3

1 point(s)

Chest wall rigidity associated with fentanyl: (select all that apply)

- ☑ May be mediated by the gamma-aminobutyric acid at the spinal cord and basal ganglia
- ☑ Occurs at doses that exceed 5 mcg/kg
- ☑ May necessitate emergent intubation and neuromuscular paralysis due to laryngospasm
- ☑ Can be mitigated by administration via slow IV push

Correct

Chest wall rigidity associated with fentanyl generally occurs at doses that exceed 5 mcg/kg, and occurs more commonly in the pediatric population relative to adults. It is hypothesized that this effect occurs as a result of the binding of fentanyl to the mu and kappa receptors at the spinal cord and basal ganglia, which is controlled through the gamma-aminobutyric acid (GABA) pathways at these sites. Naloxone may not lead to complete antagonism of this phenomenon. Laryngospasm associated with fentanyl may necessitate neuromuscular paralysis and emergent intubation. Chest wall rigidity can be avoided by administering intravenous fentanyl over a period of three to five minutes followed by adequate flushing of the intravenous line tubing in a slow and cautious manner.

Fentanyl and Midazolam

Question 2 of 3

1 point(s)

A 37-year-old female with a history of asthma, epilepsy, and IV drug use presents to the emergency department for incision and drainage of a large abscess on her shoulder. Patient is in extreme pain and procedural sedation is warranted. Which of the following agent(s) are most appropriate for this patient?

- ○ Etomidate
- ◉ Ketamine and propofol
- ○ Methohexital
- ○ Fentanyl and midazolam

Correct

Of the agents listed, the combination of ketamine and propofol may be the most appropriate combination in this patient. Myoclonus is an adverse effect associated with etomidate, and although it is not an absolute contraindication for use in patients with a history of epilepsy, propofol or ketamine (or both agents) may be more suitable agents to use for procedural sedation in such patients. In patients with a history of asthma who are undergoing procedural sedation, agents should be selected that pose minimal risk of respiratory depression. Both the combination of fentanyl and midazolam as well as methohexital are associated with respiratory depression, making the use of ketamine and propofol an ideal combination for use in this patient.

Fentanyl and Midazolam

Question 3 of 3

1 point(s)

An agitated six-year-old 20-kg girl presents with a foreign body in her ear. She requires procedural sedation in the emergency department for foreign body removal, but has no intravenous access. You decide to use midazolam to calm the patient and visualize the foreign body. Which of the following regimens describes the most appropriate dosage and route of administration in this patient?

- (●) 1 mg midazolam IM
- ( ) 10 mg midazolam PO
- ( ) 4 mg midazolam IN

Correct

Of the options listed, the intramuscular route of administration of midazolam at a dose of 0.05 mg/kg (typical dose ranges between 0.025 mg/kg to 0.1 mg/kg IM) for this patient is the most appropriate. Oral administration of midazolam at a dose of 0.5 mg/kg has an onset of action of 30 minutes, and may lead to unreliable sedation due to first-pass metabolism. The intranasal route of administration of midazolam is 0.2 mg/kg, but may not be well-tolerated in patients who are crying or agitated.

FINISH QUIZ

Dexmedetomidine

Description

Dexmedetomidine is a newer sedative agent initially approved in 1999. Dexmedetomidine's labeled indications include adult ICU sedation and procedural sedation. [1] While dexmedetomidine has been studied for different procedures and indications (e.g., alcohol withdrawal), experience in emergency medicine is limited. [2]

Dexmedetomidine is a "clonidine-like" medication that is seven times more potent than clonidine. Dexmedetomidine is an agonist at the alpha-2 receptor in the brain stem, decreasing systemic circulation of catecholamines resulting in sedation, anxiolysis, and mild analgesia. [3] One advantage of dexmedetomidine is that it does not cause significant respiratory depression. [1–5] Dexmedetomidine's most concerning adverse events are bradycardia and hypotension that can occur in up to 14% and 54% of patients respectively. [1] With high infusion rates or loading doses, dexmedetomidine may also cause initial peripheral vasosconstriction resulting in transient hypertension. [3,4]

Contraindications

None listed by the manufacturer, but caution should be exercised in patients with hypovolemia, chronic hypertension, advanced heart block, severe ventricular dysfunction or the elderly. [1]

Experience in Emergency Medicine

In the emergency department dexmedetomidine experience has been mostly limited to pediatric pateints and non-painful procedures. A review of dexmedetomidine use for sedation during imaging studies (e.g, MRI/CT scans) found moderate success. [3] However, many patients in this review received pre-medication or additional sedative boluses during the procedures. In one study, dexmedetomidine was used for sedation during pediatric cardiac catheterization with 60% (12/20) of kids requiring additional propofol for excessive movement. [1] A review of limited literature suggests that combination of ketamine and dexmedetomidine may offset the adverse events associated with each drug; however, experience with this approach remains to be evaluated in the emergency department. [4]

From an emergency medicine perspective, the disadvantages of dexmedetomidine are:

- Lack of deep sedation and analgesia at recommended doses resulting in poor success for painful/invasive procedures [4]
- Long onset time
- The need for a loading dose
- The need for a continuous infusion pump
- The concern for bradycardia and hypotension with higher dosing
- Increased cost compared to other sedatives

Dosage and Administration

Dexmedetomidine dosage and administration	
Recommended IV dose (load) [1]	1 mcg/kg over 10 minutes via infusion pump
Infusion during procedure	0.6 mcg/kg/hour
Titration range	0.2 – 1 mcg/kg/hour
Onset	5 – 10 minutes
Duration	Infusion dependent

Dexmedetomidine must be infused using an infusion device. Dexmedetomidine units of dosing are error-prone as the medication is dosed per hour rather than per minute (e.g., propofol).

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