What Agent Should I Use For Procedural Sedation?
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Take Home Points

- Propofol can be used in conjunction with ketamine to minimize complications such as hypertension, muscle rigidity and emergency reaction.
- Patients may experience partial dissociation as they metabolize ketamine. This may be distressing to the patient.
- Dissociative dose ketamine may still cause hypoventilation and apnea.
- Elderly patients may require less propofol.
- Etomidate is likely to cause myoclonus as well as nausea/vomiting.

- Humanely performing painful procedures is one of the most satisfying aspects of emergency medicine. Over the last decade, we have emerged from the shadows of fentanyl/midazolam to enter the golden age of procedural sedation pharmacology. Most of us have a variety of better agents at our disposal so we don’t have to choose between agony and apnea. Ketamine, etomidate and propofol will give great results for just about every procedure about every time. To choose between them, you need to get to know them.

- Ketamine. This came into being in the 1960s when pharmacologists recognized the potential of dissociative anesthesia. The first commonly available agent in this class was phencyclidine (initially known as Sernyl and now as PCP). Dissociative anesthesia produces a state of unconsciousness that renders patients unaware and impervious to external stimuli while preserving other brain functions such as airway reflexes and cardiorespiratory tone.
  - Sernyl had a prolonged and nasty recovery period where patients often became agitated and psychotic for hours upon emergence. A variant on phencyclidine was sought. The derivative that provided dissociation with the best emergence profile was a ketone with an amine; ketamine. Ketamine is used for analgesia, RSI, agitation, asthma, alcohol withdrawal, opioid withdrawal, depression, suicidality and everything else. Its best use is for procedural sedation.
  - Ketamine has reliable pharmacokinetics from the intramuscular route which makes it of special value in veterinary and pediatric medicine.
  - Use of ketamine in adult patients was avoided until recently for fear of psychiatric distress on emergence.
  - Preventing and managing ketamine-related psychiatric distress requires an understanding of ketamine’s effects on the brain at different doses.
    - At low doses (10 mg in a normal sized adult), ketamine has powerful analgesia properties and little effect on perception or emotions.
    - As the dose is increased to 30 mg or higher, patients will develop psychoperceptual disturbances like hallucinations and feelings of unreality but they are fully aware of what is going on and conversant. This is the recreational phase of the continuum. Most will do fine and some will love it. Some will not like it, however. Patients can be reassured.
    - At higher doses, 50-70mg, you get partial dissociation, which you don’t want.
    - Full dissociation occurs at about 1 mg/kg IV or 4 mg/kg IM. Ketamine is less potent IM. The lights are on but nobody is home. The patient maintains their ABCs but is completely isolated from all external stimuli. Dissociated is awake but unconscious. This is the desired state for painful procedures.
You can bypass the analgesic, recreational and partially dissociated stages by using a higher dose of 2mg/kg IV. However, you can’t prevent the patient from passing back through these states as they metabolize the drug on emergence, which is why psychiatric distress occurs on emergence. If you give an induction dose and the patient starts freaking out before the procedure, this means you haven’t achieved full dissociation and you should give more ketamine.

- **How someone feels as they emerge from ketamine depends on how they feel going into it.** Make them comfortable prior to induction. If the patient is in pain, treat it. Anticipatory guidance is essential. Pre-induction coaching effectively prevents psychiatric distress. **Tell the patient they will have vivid dreams and that they can choose their dreams.**

  - **Ketamine activates but disconnects the mind.** You can’t reconnect the mind. You have to wait for the patient to metabolize through partial dissociation. However, you can deactivate the mind while the patient is metabolizing using a conventional sedative. A small dose of a benzodiazepine will work great. Strayer has moved to propofol for this indication.

  - **Propofol also helps with some of the other problems that can arise with ketamine like hypertension.** Ketamine is a weak sympathomimetic. Some patients can’t tolerate this. A 58 year old patient with coronary artery disease and prior valve replacements receiving ketamine to facilitate wrist arthrocentesis had a jump in her blood pressure to 230. She then developed acute fulminant pulmonary edema and cardiac arrest. She was appropriately treated and recovered.


- **If you don’t like how high the blood pressure or heart rate is going during procedural sedation with ketamine, give a dose of propofol.** This is a sympatholytic and direct vasodilator. Propofol is great for muscle rigidity which may be seen occasionally. Ketamine also occasionally causes hypersalivation or a confluent truncal rash that is not allergic and does not require treatment. Nausea is common and effectively treated with ondansetron.

- **Do emerging patients become unconscious with propofol?** No. They usually just chill out with small dose. They may lapse into brief unconsciousness but rapidly recover. The duration of action is at most 5 minutes.

- **What dose of propofol does Strayer use?** 30-40 mg below 50 years old and decrease with advancing age.

  - **Dissociative dose ketamine can cause hypoventilation and apnea by a variety of mechanisms.** If ketamine is pushed rapidly as an intravenous bolus, you will often see a transient period of apnea that usually lasts 10-20 seconds and resolves without treatment. Give ketamine slowly. This may be done by putting your dissociative dose in a bag of 50 mL normal saline and dripping it in over 1-2 minutes. There is some evidence that psychiatric distress is less likely with longer infusion times.

  - **Dissociated patients may develop hypoventilation due to airway malpositioning, excessive salivation and laryngospasm.** These patients must be monitored by an airway capable provider. Most tolerate it well.

- **Propofol is so adept at causing hypotension, hypoventilation and apnea that these physiologic derangements are the norm when propofol is used for deep sedation.** However, propofol when used properly confers a high degree of safety from its vanishingly short duration of action.

  - **There are multiple ways to use propofol.** You can start a drip and titrate the rate to the depth of sedation desired. However, this requires patience. You may give repeated small boluses (about 20-30 mg in a normal sized adult) and hope to achieve an anesthetic homeostasis. However, propofol disappears so quickly that it becomes challenging to get and keep your patients sedated. If you give repeated doses, you are pushing the patient in and out of very deep levels of unconsciousness. **Be careful with repeated doses of propofol.**

  - **Propofol should be reserved for brief procedures and administered in a single dose.** Tank the patient up with oxygen and quickly push a bolus of propofol that is likely to lead to deep unconsciousness and possible apnea. Then the patient rapidly regains consciousness.

  - **For patients under age 50, you can give a push of 1 mg/kg followed by a quick flush and have the patient slowly count to 20.** If this doesn’t get you where you to need to be in 60 seconds, give a second push of 0.5 mg/kg. If you need more than that or the procedure is longer than expected, you can give subsequent doses of 0.25-0.5mg/kg. If you are pushing the patient to deep sedation, be careful with more than 2-3 doses of propofol.
They found that on average, lower doses were needed with advancing age. Younger patients on average needed more. Patients between 18-40 years needed 2 mg/kg. 41-64 year olds needed 1.7 mg/kg. Patients 64 and over needed 1.2 mg/kg. These probably won’t be the starting doses but may be the ending doses.

Propofol does not have analgesic properties but rapidly and effectively causes coma where patients feel no pain. While giving opiates or pain medication prior to sedation with propofol may decrease the amount of propofol necessary, giving opiates along with propofol does not help and increases the likelihood of adverse events.

Older patients can be remarkably sensitive to propofol. Use small doses for the small, frail elderly patient. Start with 20-30mg.

Ketamine and propofol play well together. Propofol causes hypotension and ketamine causes hypertension. Ketamine causes hypertonicity and nausea while propofol causes flaccidity and is an anti-emetic. Because of this synergy and the prospect of using lower doses of both agents, using them together is a great idea. There is increasing evidence supporting the safety and efficacy of ketofol. Most of literature shows that combining ketamine and propofol in the same syringe does no better than either one alone.

Dosing ketamine and propofol together in a fixed ratio doesn’t make much sense pharmacokinetically. Propofol is metabolized in minutes while ketamine accumulates. Depending on how you mix them, the propofol effects dominate for short procedures and the ketamine effects dominate for long procedures. No one has figured out the right ratio. It is better to dose them independently.

- Etomidate. Unlike ketamine which is hemodynamically stimulating and propofol which is hemodynamically depressing, etomidate is hemodynamically neutral. This is very attractive for sicker patients who are less likely to tolerate hypertension or hypotension. The dose in RSI is 0.3 mg/kg and the procedural sedation dose is about half that. 0.1-0.2 mg/kg.

- Etomidate works immediately and lasts somewhere between propofol and ketamine depending on the dose. However, etomidate is messier than propofol or ketamine. If you use it regularly, you will see a lot of myoclonus. This may be disruptive or mistaken for a seizure. Etomidate lowers the seizure threshold. This is the induction agent preferred by anesthesiologists to prolong seizures for electroconvulsive therapy.

- Etomidate may cause severe muscle rigidity including jaw rigidity as well as apnea. This is not a problem if given prior to a paralytic for RSI but is a problem for procedural sedation.

- Etomidate is the most emetogenic agent. Post-procedural nausea-vomiting are common and may be severe with etomidate.

- However, many providers love etomidate and use it routinely and effectively.

- Many providers continue to use a combination of fentanyl and midazolam. However, the onset is 3-5 minutes. This is much longer than expected. When doctors are not comfortable with these agents, they push dose after dose and then do the procedure with the patient screaming. They walk away just as the fourth dose hits its peak effect. Fortunately, there is a reversal agent. If this is all you have, go slow, have a time set to four minutes and have naloxone and flumazenil on the ready.

- There is evolving literature on newer agents such as remifentanil or dexmedetomidine. Most of this is not based in emergency medicine.

- Remifentanil is an ultra short-acting, non-accumulating opioid that produces moderate sedation and analgesia. Optimal dosing strategies and indications for ED based sedation have not been established. Remifentanil may have a role for less painful procedures when deep sedation is not required or to facilitate propofol PSA, allowing smaller doses of propofol. In the anesthesia literature, it has relatively high rate of adverse effects. Be careful.

- Dexmedetomidine is a sympatholytic alpha-2 agonist similar to clonidine but much more sedating. This produces sedation and analgesia without respiratory depression but with predictable bradycardia and sometimes hypotension. This may have its best role facilitating non-painful procedures in kids like radiology studies or as an adjunct to ketamine. As monotherapy, its more complicated dosing, slower onset and price have limited its role downstairs in the ED.
How do you choose an agent?

- **Physiologic reserve.** Propofol should be avoided when hypotension and respiratory depression are a concern. Ketamine should be avoided when hypertension or tachycardia are a concern. If your patient is brittle and you need hemodynamic neutrality, choose etomidate. Although you should always be prepared for RSI with procedural sedation, be particularly ready if using etomidate. If you are very concerned about the patient's reserve, don't forget to ask yourself if you should be doing the procedure in the emergency department at all.

- **Duration of the procedure.** Propofol for very brief procedures, especially where muscle relaxation is required. Propofol is terrific for cardioversions or lancing an abscess. For longer procedures, use ketamine. Strayer uses full dissociative dosing at least 1.5 mg/kg IV or 5 mg/kg IM and draws up 100 mg of propofol in a syringe so you can deliver a small bolus to manage hypertension, muscle rigidity or psychiatric distress.