

Clinical Practice Advisory: Emergency Department Procedural Sedation With Propofol

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We present an evidence-based clinical practice advisory for the administration of propofol for emergency department procedural sedation. We critically discuss indications, contraindications, personnel and monitoring requirements, dosing, coadministered medications, and patient recovery from propofol. Future research questions are considered. [Ann Emerg Med. 2007;50:182-187.]

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INTRODUCTION

The use of propofol in the emergency department (ED) for procedural sedation was first described in 1996 by Swanson et al¹ and then by Havel et al² in 1999. In an editorial accompanying the latter report, Green³ characterized the practice as “not yet ready for prime time.” However, in the decade since the Swanson et al seminal report, a substantial body of peer-reviewed clinical evidence has emerged that supports a more current characterization of ED propofol as both safe and efficacious (see Appendix E1, available at <http://www.annemergmed.com>).^{1,2,4-17}

A clinical practice guideline addressing the use of ketamine for ED dissociative sedation has been published.¹⁸ Sufficient data exist to establish a similar advisory for propofol.

Why a Clinical Practice Advisory for Propofol?

There are multiple clinical guidelines, review articles, and policies describing a general approach to ED procedural sedation and analgesia.¹⁹⁻²² Like all nondissociative sedatives, propofol induces dose-dependent, progressive alterations in awareness. Depending on the specific point achieved along this sedation continuum, propofol can readily produce both moderate and deep sedation, as defined by the Joint Commission on Accreditation of Healthcare Organizations.²³

There are a number of compelling reasons for a propofol-specific clinical practice advisory. Unlike longer-acting agents such as fentanyl and midazolam, propofol is ultrashort acting and can induce rapid swings in consciousness. Accordingly, propofol requires special handling and attention relative to more traditional agents, which is of particular importance in that propofol is now arguably the most popular deep sedative in emergency medicine. Finally, as a relatively new agent in our setting, with a rapidly growing body of literature supporting, defining, and refining its use, we see widespread practice variation, especially in terms of dosing, fluid pretreatment,

supplemental oxygen, monitoring adjuncts, and optimal depth of sedation.

Explanation of Clinical Practice Advisory Content

Objective. To provide evidence-based recommendations for the use of propofol in ED deep procedural sedation.

Indications

The literature supports the safety and efficacy of propofol for a variety of ED procedures requiring deep sedation, including fracture and dislocation reduction, incision and drainage of abscesses, and cardioversion.^{1,2,4-17,24-29} There is no ED experience using propofol for minimal sedation and limited experience for moderate sedation in the ED.^{9,10,30} Propofol is a suboptimal choice for these indications because of the difficulties of staying within these specific sedation ranges.⁹ Although propofol has been widely used for longer procedures in the operating room and ICU, there is insufficient experience to support its safety for longer ED procedures.

Contraindications

Propofol is contraindicated in any patient with known or suspected allergy to propofol, eggs, or soy products.³¹

Higher-Relative-Risk Patients

Age. Lower doses of propofol are required to achieve a defined endpoint in patients older than 55 years and in debilitated patients,³¹ likely because of higher peak serum levels rather than age-related changes in pharmacokinetics or brain sensitivity.^{32,33} The hypotensive effect of propofol has been found to be more pronounced with advanced age, even at similar peak serum levels.³² In a large ED study, the average age of patients experiencing oxygen desaturation or requiring assisted ventilation was 11 years higher than those without these

complications, supporting an advanced age predisposition to airway and respiratory adverse events.⁵ The distribution and clearance of propofol in children are noted to be similar to that in adults.³¹⁻³³

Underlying Medical Condition

Patients with more than minor underlying illness (ie, American Society of Anesthesiologists' physical status score III or IV) are at an increased risk of propofol-induced hypotension and other complications compared to healthier patients.^{12,22,31,34,35} Propofol-associated hypotension has a duration similar to its sedative effects and is exacerbated by volume depletion.^{31,36-40}

Patients with depleted intravascular volume, such as those patients with dehydration or blood loss, are a higher risk group for propofol-associated hypotension during sedation and should ideally have their volume optimized before the procedure.^{12,36,39}

Fasting State

There is insufficient evidence to support any specific fasting requirements before procedural sedation, regardless of depth achieved or agent administered. These issues have been discussed in detail elsewhere and are beyond the scope of this advisory.⁴¹⁻⁴⁴ When administering any procedural sedation, emergency physicians must balance the relatively low probability of aspiration with the patient's underlying risk factors, the timing and nature of recent oral intake, the urgency of the procedure, and the depth and length of required sedation.

Personnel

The standard ED sedation team includes 2 individuals: a nurse dedicated to patient monitoring and an emergency physician performing the procedure while prepared for resuscitation if required.²¹ Emergency physicians are, by the nature of their residency training, qualified to administer deep sedation and prepared to rescue patients from inadvertent or excessive sedation. The specific controversy with ultrashort-acting agents such as propofol is whether there should be an emergency physician separate from the procedure who is wholly dedicated to drug administration and patient monitoring.

The warning section of the package insert for propofol states that caregivers "not involved in the conduct of the surgical/diagnostic procedure" should administer propofol during sedation or anesthesia.³¹ Indeed, the majority of existing ED series use a separate emergency physician not involved in the procedure,^{4,5-8,14,25} according to the premise that the rapid swings in the level of sedation and the cumulative sedation depth might lead to avoidable complications if the supervising physician is distracted by the procedure. Despite this, a recent report describes 1,028 ED sedation encounters (24% using propofol) in which a single physician simultaneously supervised sedation and performed the procedure.⁴⁵ Adverse event rates were similar to those reported for 2-physician sedation. In non-ED settings, propofol is widely and safely administered by a

single physician and nurse.⁴⁶⁻⁴⁸ Although it is difficult to extrapolate results from elective procedures performed in controlled situations to the ED setting, there is no current evidence to suggest that propofol is unsafe without a second physician present. Nevertheless, the provision of an emergency physician dedicated to sedation oversight seems prudent whenever feasible.

Pre-sedation

Patients receiving propofol should first undergo a standard pre-sedation assessment,^{21,49} including a review of absolute and relative contraindications to propofol.

Propofol Administration: Pharmacology

Although individual patient response will vary, the sedative effects of propofol are typically dose dependent.^{50,51} The onset of clinical sedation is usually within 30 seconds from injection. The half-life for propofol blood-brain equilibration is approximately 1 to 3 minutes, and clinical effects typically resolve within 6 minutes. The total sedation duration depends on the quantity and timing of initial and repeated dosing.³¹

Plasma propofol levels decrease rapidly after administration from both rapid distribution and high metabolic clearance. Distribution accounts for approximately half of the serum level decrease after a propofol bolus.³¹ As body tissues equilibrate with plasma and become saturated, distribution of remaining serum propofol is delayed. Therefore, propofol will be cleared more quickly with the initial bolus than with subsequent doses. Propofol is eliminated by hepatic conjugation to inactive metabolites that are excreted by the kidney, with a metabolic rate of 25 to 50 mg/kg per minute in a 70-kg adult.^{31,52,53}

Standard propofol doses used by anesthesiologists to induce general anesthesia are 2.0 to 2.5 mg/kg intravenously in adults and 2.5 to 3.5 mg/kg intravenously in children.³¹ In contrast, the most common doses studied in the ED setting are an initial bolus of 1.0 mg/kg, followed by 0.5 mg/kg every 3 minutes as needed to achieve or maintain sedation (same in adults and children).^{4-9,12,25}

Higher doses than 1.0 mg/kg appear to be associated with higher rates of respiratory depression. In a pediatric ICU study, Vardi et al⁵⁴ administered loading doses of 2.5 mg/kg, followed by 1 mg/kg boluses as needed, to 58 children and noted the need for assisted ventilation in 10 and hypotension in 6. Barbi et al⁵⁵ administered up to 2.0 mg/kg of propofol to children receiving gastroenterology procedures and noted oxygen desaturation in 21.4%. A loading dose of 1 mg/kg bolus, followed by an unspecified "seamless" administration of small propofol aliquots, to a total dose of 4.5 mg/kg during the course of the sedation has been described in children as well.²⁵ There was no correlation between the number of doses received and the complications observed in this study, although the oxygen desaturation rate reported was a relatively high 30.5%. In the original ED report by Swanson et al,¹ a continuous infusion of 0.21 mg/kg per minute, titrated to the desired sedation level,

resulted in procedural recall in 7 of 20 (35%) patients and desaturation events in 2 of 20 (2.5%) patients.

Until further trials have been reported comparing propofol dosing strategies for nonintubated patients, an initial bolus dose of 1 mg/kg, followed by 0.5 mg/kg every 3 minutes as needed, appears to be safe and effective for ED adults and children.

Propofol Administration: Clinical Effect

Propofol is not an analgesic and serves only as a sedative and amnestic. The clinical significance of procedural pain that a patient experiences but cannot later recall remains unclear. Amnesia lasts an average of 15.7 minutes in adults who have received 1 mg/kg of propofol followed by 0.5 mg/kg until sedated.⁵⁶ Low rates of patient-reported pain or recall have been found in ED propofol studies (10% to 12%),⁸⁻¹⁰ although the patients in these studies all received narcotic analgesics before the start of their procedure. Administering combinations of propofol concurrently with analgesics may increase the likelihood of adverse outcomes,^{57,58} and most of the medications used for analgesia in the ED have half-lives that are significantly longer than the 2- to 4-minute initial redistribution half-life of propofol, making concurrent administration unnecessary. Unlike midazolam and fentanyl, which are classically titrated together, propofol should be administered as a sole agent after complete or near-complete analgesia has been achieved with an opiate.^{8-10,12,56}

Interactive and Mechanical Monitoring

As with all moderate and deep sedation, patients receiving propofol should be monitored continuously to assess level of consciousness and to identify the early signs of hypotension, bradycardia, apnea, airway obstruction, or hypoventilation.²¹ The patient's airway should be observed at all times until the patient has recovered. Patients who require surgical drapes should ideally have them positioned in such a manner that chest motion from breathing can still be observed. Both mechanical monitoring and direct visualization are required to detect all changes in respiratory effort or the patient's level of consciousness.^{9,11,58}

Continuous pulse oximetry is a routine monitoring modality for all ED sedation (including propofol) and will effectively detect hypoxemia associated with hypoventilation, apnea, or airway obstruction.^{20-22,58}

End-tidal carbon dioxide, capnography, can be used to detect changes in a patient's respiratory pattern, such as airway obstruction, hypoventilation, and apnea, during procedural sedation.^{11,15,57,59-61} Indeed, it appears that capnography can reliably detect these events earlier than either clinical examination or pulse oximetry. Capnography represents an enhanced means of assessing a patient's respiratory status and should be considered during procedural sedation with propofol.

Supplemental Oxygen During Propofol Sedation

The use of supplemental oxygen throughout procedural sedation is a common ED practice. The benefit is that enhanced

oxygen reserves permit a longer period of normal oxygenation in the event of apnea or respiratory depression. The disadvantage is that supplemental oxygen therefore negates oximetry as an early warning device.^{11,57}

Jurell et al⁶² compared patients receiving midazolam and meperidine for endoscopy according to the use or nonuse of supplemental oxygen and noted markedly less desaturation in the oxygen group (8% versus 44%). Two studies of ED propofol sedation without supplemental oxygen have reported desaturation rates of 11.6% and 31%.^{7,25} These rates are higher than the 5% to 7% similarly observed in studies with supplemental oxygen.^{4-6,10,12}

A recent randomized, controlled trial showed no apparent benefit to supplemental oxygen during ED moderate sedation⁶³; however, this question has not been similarly studied for deep sedation. In the case of apnea, a preoxygenated patient will tolerate a longer period of apnea without requiring assisted ventilation, with the associated risk of gastric insufflation. Thus, although unproven, the administration of supplemental oxygen with propofol seems prudent, particularly when the patient's respiratory status can be monitored with capnography, in addition to pulse oximetry.

Potential Adverse Effects

Potential adverse events associated with ED propofol use include lack of adequate sedation; oversedation; hypoxemia; respiratory depression, including hypoventilation; airway obstruction and apnea; respiratory arrest; hemodynamic instability; nausea; emesis; pain with injection; and unplanned admission as a result of adverse events encountered. These events are not unique to propofol but are typical for moderate and deep sedation. The frequency of adverse events, such as hypoxemia, apnea, airway obstruction, cardiovascular events, and emesis, related to moderate and deep sedatives would appear to be less than 5% of patient sedations, including those with propofol.^{4-12,25,64,65} These events have been readily addressed with brief interventions (eg, supplemental oxygen, jaw thrust, assisted ventilation, and intravenous fluid administration) and have not been characterized as requiring more extensive interventions or incurring serious patient sequelae.

Respiratory Depression

The frequency and type of adverse respiratory events attributed to adult ED propofol use have been similar to those reported in children.^{1,5,8,10,12,15,24,25} The use of bag-valve-mask-assisted ventilations has been described to occur in 3.0% to 9.4% of patients. These ranges are listed in the [Table](#).

Hypotension

Transient hypotension is an expected response of a propofol bolus and can be pronounced in patients with depleted intravascular volumes.^{31,36,52} Miner et al¹² noted mean systolic blood pressure decreases of 17.1% after propofol in patients

Table. Overview of selected studies of ED procedural sedation and analgesia with propofol (studies in the ED using an initial dosing strategy of 1 mg/kg bolus, followed by smaller aliquots of propofol as needed).

Authors	Pediatric or Adult	Oxygen Desaturation, %	Bag-Valve-Mask Use, %	Preprocedural Supplemental Oxygen
Anderson et al ¹⁵	Pediatric	4.8	3.2	Yes
Bassett et al ⁴	Pediatric	5	0.8	Yes
Burton et al ⁵	Both	7.7	3.9	Yes
Guenther et al ⁷	Pediatric	7	1	Yes
Godambe et al ²⁵	Pediatric	31	0	No
Havel et al ²	Pediatric	11.6	0	No
Miner et al ⁸	Adult	10.6	3.9	57% Of patients
Miner et al ¹⁰	Adult	7.0	1	Yes
Miner et al ¹²	Adult	6.4	3.2	Yes
Miner et al ¹⁴	Adult	9.1	4.6	80% Of patients

with substantial underlying illness. Mean decreases in systolic blood pressure of 21 mm Hg and 10.5 mm Hg were found in the Bassett et al⁴ and Guenther et al⁷ studies of healthy children. In a recent series, Burton et al⁵ noted that only 3.5% of 792 ED propofol patients experienced blood pressure decreases of greater than 20%, and each of these occurrences resolved promptly and without sequelae.

Pain With Injection

Injection site pain with propofol is uncommon in existing ED reports (2% to 20%).^{1,4-11,13,24,56} As a consequence, no strategies to mitigate such discomfort have been reported in our setting. Postprocedural recall of injection pain has been found in as many as 70% of postoperative patients.⁶⁶ One described technique that prevents such discomfort 60% of the time is the administration of 0.5 mg/kg intravenous lidocaine with a rubber tourniquet in place 30 to 120 seconds before propofol administration.⁶⁶ Another study compared 2 other interventions—the administration of alfentanil 1 mg intravenously before propofol or lidocaine 0.5 mg/kg mixed with the propofol bolus—and noted 10% and 24% recall of injection pain, respectively, compared to 67% with placebo.⁶⁷ Given that the use of lidocaine represents no significant harm to patients, emergency physicians wishing to mitigate propofol injection pain may consider one of the above interventions.

Recovery and Discharge

As with any procedural sedation, patients should be monitored until they have returned to their baseline mental status. The exact timing of patient observation before discharge will be variable because of the nature of propofol redistribution and the clinical circumstances. The redistributive nature of propofol suggests that patients who have regained their baseline level of consciousness after propofol administration will be unlikely to have further decreases in their level of consciousness and therefore are unlikely to exhibit any new adverse events. The occurrence of adverse events after discharge in ED patients treated with propofol sedation has not been reported. Discharge criteria and instructions do not need to differ from those elements appropriate for ED patients in general.

Future Research Questions

Future studies should continue to assess optimal dosing strategies for ED propofol, including potential differences based on age, underlying illness, and specific procedures. The impact of additional monitoring modalities on the incidence of propofol-related respiratory events should be further considered. Existing evidence suggests that capnography can identify respiratory and airway adverse events before clinical examination and pulse oximetry, and future research should investigate whether this tool can affect clinically important propofol outcomes such as the incidence of assisted ventilation.^{11,57,59}

Other research of interest would be the identification of predictors of adverse events, the impact of supplemental oxygen, interventions to mitigate injection pain, and interventions to minimize propofol-induced hypotension. Finally, larger studies than those presently available will be required to more precisely verify the incidence and magnitude of adverse events associated with ED propofol.

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CORRECTION NOTICE

In the June 2007 issue, in the editorial by Erdman, ("Is Hydroxocobalamin Safe and Effective for Smoke Inhalation? Searching for Guidance in the Haze", pages 814-816), reference is made to Cyanokit® consisting of amyl nitrite, sodium nitrite and sodium thiosulfate. These are the components of the cyanide antidote kit, **not** Cyanokit®. Cyanokit® consists of 5 grams of lyophilized hydroxocobalamin packaged as two 2.5 gram vials. We regret the error.

APPENDIX E1.

Clinical practice advisory for ED propofol procedural sedation.

OBJECTIVE

To present an evidence-based clinical practice advisory for the administration of propofol for ED procedural sedation.

INDICATIONS

Brief, painful procedures in which deep procedural sedation is indicated, including fracture and dislocation reductions, incision and drainage of abscesses, cardioversion, tube thoracostomy, and central line placement.

CONTRAINDICATIONS

Absolute (risks essentially outweigh benefits):

Known or suspected allergy to soy or eggs.

Higher-relative-risk patients (risk and benefit should be considered):

Patients who are older than 55 years, are debilitated, or have more than minor underlying illness (ie, ASA physical status score III or IV) are at an increased risk of propofol-induced hypotension and other complications. When the benefits of using propofol outweigh the greater risk in these patients, administer lower doses more slowly. Patients should ideally have their volume status optimized before receiving propofol.

As with deep sedation using any agent, there is no clear consensus about the optimal fasting time before sedation. Such decision-making should balance the relatively low probability of aspiration with the patient's underlying risk factors, the timing and nature of recent oral intake, the urgency of the procedure, and the depth and length of required sedation.

PERSONNEL

As with any ED deep sedation, the minimum personnel present during the sedation should be an emergency physician and ED nurse. Most institutions favor the use of a separate emergency physician uninvolved in the procedure who is dedicated to drug administration and patient monitoring.

PRESEDATION

Physicians should perform a standard pre sedation assessment, with greater attention than usual to the potential for airway management, given the typical endpoint of deep sedation.

As with all procedural sedation, suction, airway, and resuscitation equipment should be immediately available.

Unless precluded by the urgency of the procedure, it is recommended that intravenous opioids be administered to patients with acutely painful conditions such that complete or near-complete analgesia is attained before propofol sedation.

PROPOFOL ADMINISTRATION: GENERAL

Propofol induces sedation approximately 30 seconds after bolus injection, with typical resolution of clinical effects by 6 minutes after administration.

The most ED experience is with an initial bolus dose of 1 mg/kg, followed by 0.5 mg/kg every 2 to 3 minutes as needed to achieve or maintain the desired level of sedation. This dosing is the same in adults and children.

Propofol is typically titrated to slurring of speech or lid ptosis, depending on the depth of sedation and degree of relaxation needed for the procedure.

INTERACTIVE AND MECHANICAL MONITORING

As with any ED deep sedation, patients should have their airway patency, oxygen saturation, electrocardiogram tracing, and level of consciousness continuously monitored.

The optional addition of end-tidal carbon dioxide monitoring (capnography) can provide warning of impending airway and respiratory complications before clinical examination or pulse oximetry.

Although proof of its benefit is thus far lacking, the administration of supplemental oxygen throughout propofol sedation may decrease the need for or duration of assisted ventilation should respiratory depression or apnea occur. Such oxygen administration will also delay the detection of airway or respiratory adverse events by pulse oximetry.

POTENTIAL ADVERSE EFFECTS

Respiratory depression or apnea leading to assisted ventilation (0% to 3.9%)

Transient hypotension (2.2% to 6.5%)

Emesis (0% to 0.5%)

Pain with injection (2% to 20%)

RECOVERY AND DISCHARGE

As with any procedural sedation, patients receiving propofol should be monitored until they have returned to their baseline mental status.

Qualified personnel should accompany patients who require transport before recovery.