

Clinical Practice Guideline for Emergency Department Procedural Sedation With Propofol: 2018 Update



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We update an evidence-based clinical practice guideline for the administration of propofol for emergency department procedural sedation. Both the unique considerations of using this drug in the pediatric population and the substantial new research warrant revision of the 2007 advisory. We discuss the indications, contraindications, personnel requirements, monitoring, dosing, coadministered medications, and adverse events for propofol sedation. [Ann Emerg Med. 2019;73:470-480.]

A **podcast** for this article is available at www.annemergmed.com.

0196-0644/\$-see front matter

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<https://doi.org/10.1016/j.annemergmed.2018.12.012>

INTRODUCTION

The use of propofol in the emergency department (ED) for procedural sedation was first described in 1996 by Swanson et al.¹ In the intervening 2 decades, substantial peer-reviewed clinical evidence established propofol as both a safe and efficacious option for ED procedural sedation.

Because of recognition of the unique characteristics of propofol as an ultrashort-acting agent, its rapidly increasing popularity despite being a relatively new agent in the ED setting, and widespread practice variation in its use, a clinical practice advisory was published in 2007 to provide evidence-based recommendations for its use.²

An updated clinical practice guideline (Figure) is warranted for 3 reasons. First, the initial advisory focused on the use of propofol in the ED across all ages, with limited focus on pediatric patients. Use of propofol in the ED for pediatric patients is newer, and more recent literature suggests that there are unique dosing and oxygenation considerations for children. Second, a significant body of research published since the 2007 advisory has further underscored the safety of ED propofol use, such that the most recent guidelines on procedural sedation and analgesia from the American College of Emergency Physicians (ACEP) recommend propofol as a safe sedative for both children and adults, with the highest level of evidence.³ Despite the increasing body of literature and strong endorsement from ACEP, propofol use is significantly lower in pediatric patients than in adults.^{4,5} Third, the previous clinical practice advisory did not address the increasingly common practice of coadministration of other medications such as ketamine or fentanyl with propofol. In the intervening years, substantial research has explored the safety and efficacy of this practice.³

MATERIALS AND METHODS

We assembled a clinical practice advisory update committee of emergency physicians with clinical experience and research expertise in the use of propofol, including the authors of the previous version. We limited the panel to emergency physicians because the ED setting is the exclusive focus of this guideline.

To perform this update, we searched PubMed from January 2007 to July 2018 for literature on the use of propofol in children and adults. We primarily focused on the ED setting, but also reviewed relevant anesthesia literature from both inside and outside the operating room setting. We subsequently searched the reference lists of identified articles for additional relevant articles.

EXPLANATION OF CLINICAL PRACTICE GUIDELINE CONTENT

Our objective was to provide evidence-based recommendations for the use of propofol in ED deep procedural sedation.

INDICATIONS

Propofol is a short-acting sedative hypnotic that satisfies the requirements for effective ED sedation as outlined by ACEP, the American Academy of Pediatrics, the Pediatric Emergency Research Canada, and the Pediatric Emergency Care Applied Research Network.⁶⁻⁸ The literature supports the safety and efficacy of propofol for a variety of ED procedures requiring deep sedation.³ The use of propofol for moderate sedation has been described and is associated with fewer adverse

<p>Contraindications and high-risk patients</p> <ul style="list-style-type: none"> • The only true contraindication is a propofol allergy. Propofol is safe for use in patients with soy or egg allergies. • Elderly patients, infants <6 mo, patients with American Society of Anesthesiologists status III or greater, and patients with depleted intravascular volume are at higher risk for complications: close monitoring, careful dose titration, and consideration of alternative regimens are recommended. <p>Fasting state</p> <ul style="list-style-type: none"> • The literature does not support a significant association between fasting length and incidence of adverse events in adult or pediatric patients. The urgency of the procedure dictates the necessity of providing sedation without delay, regardless of fasting status. <p>Personnel</p> <ul style="list-style-type: none"> • Sedation providers must be qualified to administer deep sedation and to rescue patients who experience complications. • An ED sedation team is ideally composed of 2 individuals: one provider dedicated to interactive patient monitoring and another performing the procedure; a single provider performing both the sedation and procedure must be prepared to interrupt the procedure to perform resuscitation. <p>Bolus dosing</p> <ul style="list-style-type: none"> • Adults: Initial bolus dosing of 0.5–1.0 mg/kg (start 0.5 mg/kg or less in the elderly), with additional boluses of 0.25–0.5 mg/kg every 1–3 minutes as needed 	<ul style="list-style-type: none"> • Pediatrics: Initial bolus dosing of 2 mg/kg in patients ≤3 y and 1.5 mg/kg in older children and teenagers, with additional boluses of 0.5–1 mg/kg every 1–3 minutes as needed <p>Continuous infusions</p> <ul style="list-style-type: none"> • Adults: 100–150 µg/kg per minute (6–9 mg/kg per hour) • Pediatrics: 100–250 µg/kg per minute (6–15 mg/kg per hour) <p>Coadministration of analgesia</p> <ul style="list-style-type: none"> • Fixed-dose ketamine: ketamine at 0.1–0.5 mg/kg (dose of 0.5 mg/kg required for infants and young children), followed by titrated propofol • Single-syringe ketofol: premade mixture of ketamine and propofol within same syringe (most common is 1:1 mixture, which is dosed with the same milliliter/kilogram dosing as single-agent propofol) • Opioid coadministration: most commonly fentanyl or morphine titrated to effect <p>Monitoring</p> <ul style="list-style-type: none"> • Continuous cardiac monitoring, capnography, and pulse oximetry required for deep sedation, with respiratory rate and blood pressure recorded at least every 5 min • Supplemental oxygen recommended for both adult and pediatric patients undergoing propofol sedation <p>Adverse events</p> <ul style="list-style-type: none"> • Sedation-related adverse events with propofol include respiratory depression, hypotension, and pain with injection; these occur in ≤10% of ED sedations and typically require only minor, brief interventions, without evidence of serious patient sequelae.
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Figure. Clinical practice guideline for emergency department procedural sedation with propofol: summary of recommendations.

events than deep sedation. Targeting any given sedation endpoint with propofol is frequently associated with overshooting; thus, preparing to manage deeper levels of sedation than intended is mandatory.^{9–13}

CONTRAINDICATIONS

In the previous clinical practice advisory, propofol was contraindicated for patients with allergy to eggs or soy products. Propofol is made with soybean oil and egg lecithin, a fatty substance. Patients who are allergic to soy and eggs are allergic to the proteins, rather than the oils and fats. Although there is a theoretic risk that soybean oil or

egg lecithin could contain trace amounts of residual protein, data do not support this concern. Propofol has been safely used in adult patients with positive specific immunoglobulin E response to egg, soy, or peanut who are undergoing anesthesia, with no signs of allergic reactions.¹⁴ It has similarly been used safely in children with food allergies, with no reported cases of anaphylaxis and no increased risk of allergic reactions.^{15–18} Given this increasing body of literature, the American Academy of Allergy, Asthma & Immunology has stated that it is safe for patients with soy or egg allergies.¹⁹ Consequently, the only true contraindication to propofol is a propofol allergy.

HIGHER-RELATIVE-RISK PATIENTS

Age

Children younger than 6 months (particularly those <3 months) or weighing less than 5 kg have a higher risk of sedation-related adverse events with all sedation medications, including propofol.²⁰⁻²³ Advanced age also has been shown to predispose patients to both the hypotensive effects of propofol and the incidence of respiratory adverse events, with risk increasing after aged 50 years even at similar peak serum levels, most notably among elderly patients aged 75 years and older.²⁴⁻²⁹

Underlying Medical Condition

The majority of studies of propofol comes from healthy patients with minor underlying illnesses (American Society of Anesthesiologists physical status class I or II).³⁰ However, propofol has been used in patients with more significant comorbidities (American Society of Anesthesiologists class III or greater), and these patients have been found to have an increased risk of sedation-related complications.^{20,31,32}

Propofol-associated hypotension during sedation is observed more commonly in patients with depleted intravascular volume. For patients with a history of dehydration, blood loss, or prolonged fasting state, providers should ideally optimize volume status before sedation or consider an alternative sedation plan in persistently hypotensive or poorly perfused patients.³²

Fasting State

There is insufficient evidence to support specific fasting requirements before ED procedural sedation. The majority of the literature suggests no association between fasting length and incidence of adverse events—specifically, the risk of emesis or aspiration—in both adult and pediatric patients.^{3,33-36} We refer providers to the ACEP guidelines on fasting state and procedural sedation, which state that the urgency of the procedure dictates the necessity of providing sedation without delay, regardless of fasting status.³⁷ For patients who recently ingested a substantial meal and have risk factors for aspiration, such as younger than 12 months, obesity, obstructive sleep apnea, or serious underlying illness, providers should balance the risks and benefits to determine whether delaying procedural sedation is warranted. If delay is not possible, ED providers should target the lightest level of sedation that can be reasonably used without sacrificing patient comfort because sedation depth appears to be inversely related to the potential for adverse events, or they should consider using dissociative sedation with ketamine because protective airway reflexes

are preserved (although there is no evidence to support the safety of any particular sedation regimen over another).^{20,37}

PERSONNEL

Sedation providers must be trained and qualified to administer deep sedation and to rescue patients who achieve deeper levels of sedation than planned or experience complications. Ideally, an ED sedation team is composed of 2 individuals: one provider who is dedicated to interactive patient monitoring and another who is performing the procedure for which the patient is being sedated.^{3,6} The literature describes safe administration of ED sedation, including with propofol, by a single physician responsible for both the sedation and the procedure without an increase in adverse events.³⁸⁻⁴¹ Furthermore, in non-ED settings, there is substantial published experience with safe propofol administration by a single physician and nurse, including nurse-administered propofol sedation with a physician proceduralist.^{42,43} If the proceduralist lacks the airway management and resuscitative skills necessary to rescue a patient from inadvertent oversedation and resulting airway compromise during deep sedation, the presence of an additional provider dedicated to the sedation is necessary. In procedures performed by an emergency physician that require deep sedation, we recommend adherence to the ACEP and American Academy of Pediatrics guidelines, which stipulate that for deep sedation the physician administering sedation should not be the proceduralist except in emergency situations or in settings in which another physician with appropriate sedation skills is not immediately available.^{6,37} In situations in which a single provider is performing both the sedation and procedure, the physician must be prepared to interrupt the procedure immediately to perform resuscitation if necessary.

PRESEDATION ASSESSMENT

All patients receiving procedural sedation with propofol in the ED require a pre sedation assessment, including screening for any characteristics that make a patient higher risk for propofol sedation as detailed above.^{3,44} Such assessment may be brief or abbreviated in emergency cases.

PROPOFOL ADMINISTRATION: PHARMACOLOGY

Propofol acts on neuronal lipid membranes to potentiate activity of γ -aminobutyric acid, with near-immediate onset and brief duration. Although individual patient response varies, the onset of action is usually within 30 to 60 seconds, with blood-brain equilibration in 1 to 3 minutes and duration of action of less than 10 minutes. With initial

bolus dosing, peak effect is usually observed at 2 to 4 minutes. Plasma propofol levels decrease rapidly after bolus administration because of rapid redistribution to the periphery and high metabolic clearance. Younger children require an increased loading dose compared with adults, and redistribution occurs more rapidly in these patients because of increased metabolic clearance and larger volumes of distribution. As body tissues become saturated, distribution of serum propofol is delayed. This means the initial propofol bolus will be cleared more quickly than subsequent doses, resulting in more variable and prolonged duration of action after repeated doses. The total duration of sedation will depend on the timing and amount of initial and repeated dosing, with longer duration for procedures requiring higher total dosing.^{26,45-50}

Adults

Standard dosing is an initial bolus of 0.5 to 1.0 mg/kg, with additional boluses of 0.25 to 0.5 mg/kg every 1 to 3 minutes as needed to achieve or maintain sedation.^{24,26,51,52} Because propofol should be dosed on lean body mass, obese patients require lower total body-weight-based dosing.⁵⁰ Starting at the lower end of the dosing range (0.5 mg/kg) is also advisable in elderly patients, and a common recommendation is to use 100 minus the age as an initial dose.^{28,53}

Pediatrics

Children require higher per-kilogram dosing to achieve desired sedation levels because of a larger volume of distribution, with age inversely correlated with required loading dose. Standard initial bolus dosing of 2 mg/kg may be required in patients aged 3 years and younger, whereas doses of 1.5 mg/kg are more appropriate in older children and teenagers.^{47,54-56} These doses are tolerated without an increase in adverse effects, particularly in children aged 3 years and younger, who resume spontaneous ventilation faster after initial bolus dosing than older children.⁵⁷ In addition, children show significant interpatient pharmacokinetic and pharmacodynamic variability, with 3- to 4-fold variation in the plasma concentrations required to achieve appropriate sedation.⁵⁸ Consequently, sedation providers should be prepared to titrate additional boluses as needed to achieve effective levels of sedation in children; typically, these bolus doses will range from 0.5 to 1 mg/kg.

Infusion

There is increasing evidence in favor of use of a pump for delivery of maintenance propofol infusions.²¹ Intermittent bolus dosing produces peaks that are

associated with an increased risk of respiratory and cardiovascular depression, as well as troughs that can be associated with suboptimal sedation. This is particularly true for respiratory depression, which depends on the rate of propofol administration. With bolus dosing, onset of action of propofol is too rapid to allow a counteracting increase in plasma carbon dioxide, resulting in decreased respiratory rate or transient apnea.⁵⁹ Continuous infusions minimize such variation.⁶⁰ Maintenance infusions should be titrated between 100 and 150 µg/kg per minute (6 to 9 mg/kg per hour) to maintain adequate sedation with preserved spontaneous ventilation.⁶¹ As with bolus dosing, pediatric patients may require higher-infusion doses of up to 250 µg/kg per minute (15 mg/kg per hour).^{62,63} Such infusions are delivered through a standard infusion pump, with close attention to programming the appropriate patient dosing weight, drug concentration, and desired maintenance infusion dose. For example, to deliver 100 µg/kg per minute to an 80-kg adult, the pump should be programmed to deliver standard 1% propofol (concentration of 10 mg/mL) at 48 mL/h. Infusions are particularly beneficial in longer procedures without significant variation in the degree of painful stimulus, including complex laceration repair and postreduction casting, as well as longer imaging studies.

PROPOFOL ADMINISTRATION: CLINICAL EFFECT

Propofol has sedative and amnesic properties, but does not provide analgesia. Although there are low rates (0% to 20%) of patient-reported pain or recall among sedated ED patients, the clinical significance of procedural pain that is experienced but cannot be recalled is unclear.^{10,11,64,65}

Given the lack of analgesic properties, coadministration of propofol with analgesic agents is common. There is an increasing body of literature supporting the safety and efficacy of this practice. Whenever an analgesic is given, the provider should consider timing its administration to cover the painful portion of the procedure while minimizing the risk of respiratory depression.⁵² The 2 most common agents used with propofol are ketamine and fentanyl.

Ketamine Coadministration

Ketamine is frequently combined with propofol for painful procedures. Two methods commonly used include fixed-dose ketamine analgesia (0.1 to 0.5 mg/kg, with a dose of 0.5 mg/kg required for infants and young children) followed by titrated propofol, or a single-syringe mixture of ketamine and propofol, most commonly used as a 1:1

mixture but also used in different ratios.^{55,66-69} Dosing of ketamine-propofol single-syringe mixtures is performed with the same per-kilogram volume dosing as single-agent propofol.

When ketamine and propofol are used concurrently (often referred to as “ketofol”), deep sedation is quickly and reliably achieved, with the advantage of providing analgesia for painful procedures that is not provided by single-agent propofol and without the additional respiratory depression that can be observed with concomitant opioid analgesia.^{52,70-74} With higher ratios of ketamine to propofol, recovery time is typically prolonged compared with that with propofol alone: a 1:1 mixture of ketamine-propofol has shown a median recovery time of 8 minutes compared with 6 minutes with propofol alone.⁷⁵

Opioid Coadministration

Fentanyl is the opioid most commonly given adjunctively with propofol for painful procedures. Although the published experience with propofol-fentanyl is less robust than for ketofol, it has been shown to be as efficacious as ketofol and superior to the combination of midazolam and fentanyl in terms of facilitating a 2-fold shorter time to discharge.^{76,77} When feasible, delaying propofol administration until after the anticipated peak effect of the administered opioid is recommended. This will allow the benefit of opioid analgesia while minimizing the risk for respiratory depression and apnea that has been reported with coadministration of propofol and opioids.^{52,74}

Nonparenteral Adjuncts

Effective use of local anesthesia provides an alternative to the coadministration of ketamine or opioids with propofol. This approach is particularly applicable to complex laceration repairs, in which local anesthesia through topical, infiltrative, or regional techniques can remove the painful stimulus. Single-agent propofol can then provide excellent conditions for repair, facilitating sedation and minimizing extraneous movement. This approach can also be effectively used for lumbar punctures in children.

INTERACTIVE AND MECHANICAL MONITORING

All patients undergoing deep sedation require continuous monitoring to assess level of consciousness and to identify early signs of respiratory depression, airway obstruction, apnea, bradycardia, or hypotension.^{3,37} Both mechanical monitoring and direct visualization are needed to detect changes in respiratory effort or level of sedation, including close attention to placement of equipment, such

as sterile drapes, to ensure that the airway and chest wall can be observed as much as possible throughout the sedation.^{11,78} Mechanical monitoring for deep sedation requires continuous use of cardiac monitoring, capnography, and pulse oximetry, with respiratory rate and blood pressure recorded at a minimum of every 5 minutes.^{6,37} With uncooperative patients or young children, pre-sedation placement of the monitoring equipment may be difficult or overly distressing. In such cases, providers may plan for timely placement once sedation is achieved.

Although clinical vigilance is primary in ensuring good patient outcomes, capnography is more sensitive in detecting changes in patients' respiratory pattern, allowing the clinician to detect hypoventilation and apnea earlier than with pulse oximetry or clinical examination alone, particularly when using supplemental oxygen.⁷⁸⁻⁸⁷ The ability to detect the potential onset of adverse events earlier provides the clinician the opportunity to intervene and avert their occurrence.⁸⁵

Supplemental Oxygen During Propofol Sedation

The use of supplemental oxygen during ED procedural sedation is common. Enhanced oxygen reserves permit a longer period of normal oxygenation if a patient experiences respiratory depression or apnea. This is particularly relevant for infants and young children, who have a smaller pulmonary reserve (percentage of functional residual capacity relative to total lung volume), higher basal metabolic rate with increased oxygen consumption, and decreased ability to tolerate apnea without desaturation. Adults and adolescents who are preoxygenated with 100% FiO₂ and become apneic have a mean of 6 minutes before they experience oxygen desaturation to less than 90%. In contrast, apneic healthy children aged 2 to 12 years will desaturate to less than 90% despite preoxygenation in 3 to 4 minutes, and healthy infants will desaturate in less than 2 minutes.⁸⁸⁻⁹⁰ Among children with risk factors such as underlying pulmonary disease or concurrent respiratory infection, desaturation will occur even more rapidly.^{91,92}

The previous clinical practice advisory suggested that the administration of supplemental oxygen with propofol is prudent, arguing that preoxygenated patients tolerate longer apnea without requiring assisted ventilation. Since then, a randomized controlled trial of adults examined the use of supplemental oxygen for ED propofol sedation.⁹³ The study reported a 10% absolute decrease in the rate of hypoxia, a difference not found to be statistically significant but likely to be clinically meaningful. Stronger evidence for the utility of supplemental oxygen with propofol exists for

the pediatric population; a systematic review documented a significant decrease in the incidence of oxygen desaturation, from 17% to 10% of patients, with the use of supplemental oxygen.⁹⁴ Use of supplemental oxygen is therefore recommended for both adult and pediatric patients undergoing propofol sedation.

POTENTIAL ADVERSE EFFECTS

Sedation-related adverse events with propofol occur in less than 10% of all ED sedations and typically require only minor, brief interventions, without evidence of serious patient sequelae.^{21,24,32,35,95-99} Adverse effects associated most frequently with propofol sedation include respiratory depression, central or obstructive apnea, hemodynamic compromise, and injection pain.

Respiratory Depression

In adults, hypoxia rates with propofol range from 1% to 12%, depending on how a hypoxic event is defined.^{51,56,84,100,101} Similar variation exists for apnea and the use of bag-valve-mask–assisted ventilation, with rates ranging from 3% to 20%.^{56,100,102,103}

Despite the unique oxygenation considerations for pediatric patients, the frequency of hypoxia and apnea is the same or lower in children undergoing ED propofol sedation compared with adults. Hypoxia occurs in 1% to 9% of pediatric propofol sedations, with apnea reported in 1% to 6% of them.^{20,54,104,105}

When such events occur in either adult or pediatric patients, most resolve without incident. Significant airway interventions are rare, with the most common interventions being stimulation, airway repositioning, or the administration of supplemental oxygen. The use of bag-valve-mask ventilation is required in less than 5% of adult propofol sedations and 2% of pediatric ones.^{10,32,54,85,94,104-107} Serious adverse respiratory events are rarer still, with laryngospasm occurring in less than 1% of sedations and intubation in less than 0.1% of adult propofol sedations and less than 0.02% of pediatric ones, respectively.^{20,21,35,56,94,96,101,105}

The incidence of respiratory adverse events with ketofol compared with propofol is similar.^{51,70,75,108-110} Most adverse respiratory events during ketofol sedations are either self-resolving or responsive to minimal interventions such as airway positioning, stimulation, or increased supplemental oxygen.^{55,73,74,85,109,111}

Several studies have suggested that the combination of propofol and fentanyl has a frequency of severe hypoxia or other respiratory events similar to that of ketofol,^{21,112,113} whereas other studies have suggested higher rates of

desaturation or respiratory depression with the coadministration of fentanyl and propofol compared with ketofol.^{20,74,77,114,115} As with ketofol and propofol, most respiratory adverse events either self-resolve or require only minor intervention, with bag-valve-mask ventilation required in 1% to 2% of propofol-fentanyl sedations.^{113,114,116}

Hypotension

Reported rates of hypotension among adult patients undergoing propofol sedation range from 4% to 17%, depending on how hypotension is defined.^{24,56,100,102,103} Similar rates have been reported for pediatric patients, ranging from 2% to 15%.^{54,56,94} All reported cases are either transient and self-resolving or respond to intravenous fluid administration, without sequelae.

Transient hypotension is expected with a propofol bolus and can be more pronounced in patients with depleted intravascular volumes or substantial underlying illness.^{26,32,117-119} One of the potential advantages of combining ketamine with propofol is the reduction in the risk of hypotension, and studies of sedations performed with ketofol have found a lower incidence of hypotension compared with the incidence found with single-agent propofol.^{84,105,109,120-122} However, the clinical significance of this in otherwise healthy patients is unclear, given the transient nature of propofol-associated hypotension. The clinical significance of hypotension during sedation of the critically ill is more likely to be significant, although comparative studies of ketamine, ketofol, and propofol in this regard have not yet been published.^{32,47,67,75,103}

Pain With Injection

Although pain with injection of propofol is commonly reported in postoperative patients, it is uncommon in ED reports.^{1,10,11,24,64,78,118,119,123-125} This adverse event is particularly relevant in infants and young children, in whom agitation caused by pain with injection carries the risk of loss of the intravenous catheter. This discomfort can be mitigated through use of antecubital veins in adults. When this is not possible, one of the most effective techniques is the administration of intravenous lidocaine at 0.5 mg/kg, with a rubber tourniquet in place 30 to 120 seconds immediately before propofol administration.¹²⁶ Mixing the lidocaine dosage with the propofol bolus has also been described and may be more practical in children who will not tolerate a tourniquet.^{123,127,128} Ketofol or propofol-fentanyl, with a ketamine or fentanyl bolus administered before propofol, offers an additional option for minimizing the patients' risk of experiencing pain with injection.^{70,72,126}

Nausea, Emesis, and Aspiration

Propofol has inherent antiemetic properties, resulting in a decreased incidence of nausea and emesis compared with other sedatives, particularly ketamine.^{21,34,35,56,97} Furthermore, although agents such as ketamine can cause vomiting during recovery or after discharge, this has not been reported in ED patients receiving propofol.¹²⁹ The addition of propofol has been shown to decrease the frequency of emesis when coadministered with ketamine,^{70,72,120} with the magnitude of this antiemetic effect similar to that observed with the addition of ondansetron to ketamine sedation.¹³⁰ Emesis is similarly rare with the combination of propofol and fentanyl.^{74,112}

Given the potential loss of airway reflexes associated with propofol, aspiration is a common concern, although there is strong evidence that it is a rare occurrence. Across multiple adult studies, incidence of aspiration with propofol-based sedation is less than 0.05%.^{35,56,84,105} Large studies involving greater than 50,000 pediatric patients undergoing sedation with propofol and ketofol have documented aspiration rates between 0 and 1 in 12,500 sedations, similar to those reported for general anesthesia.^{20,21,94,105,131} Death from aspiration during procedural sedation is exceedingly rare, occurring in less than 3% of cases with documented aspiration.¹³¹

Propofol Infusion Syndrome

Propofol infusion syndrome refers to acute refractory bradycardia progressing to asystole in the presence of one or more of metabolic acidosis, rhabdomyolysis, hyperlipidemia, and enlarged or fatty liver. It has been associated with prolonged and higher-dose infusions than used for ED propofol sedations. Although there are published cases of propofol infusion syndrome occurring in ICUs and during anesthesia, no instances of propofol infusion syndrome have been reported in the ED setting.^{94,132}

RECOVERY AND DISCHARGE

Although propofol can occasionally cause idiosyncratic agitation, unpleasant recovery reactions are of little concern. Recovery agitation can occur with ketofol, although at a lesser rate than with ketamine alone. These reactions occasionally require treatment.^{72,73,109}

Patients sedated with propofol should be monitored until they return to their baseline mental status. Standard postdischarge criteria apply to propofol just as they do for any other sedative.^{3,6,35} The redistributive nature of propofol suggests that patients who regain their baseline level of consciousness after propofol administration are

unlikely to have further decreases in their level of consciousness or exhibit any new adverse events. The occurrence of adverse events after discharge in ED patients sedated with propofol has not been reported. For children, it is essential to flush the intravenous line to remove any remaining propofol at the end of the sedation. The intravenous catheter and tubing can hold a few milliliters of propofol, which can amount to a significant milligram-per-kilogram bolus dose in infants and young children.

Supervising editor: Steven M. Green, MD. Specific detailed information about possible conflict of interest for individual editors is available at <https://www.annemergmed.com/editors>.

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Authorship: All authors attest to meeting the four ICMJE.org authorship criteria: (1) Substantial contributions to the conception or design of the work; or the acquisition, analysis, or interpretation of data for the work; AND (2) Drafting the work or revising it critically for important intellectual content; AND (3) Final approval of the version to be published; AND (4) Agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Funding and support: By *Annals* policy, all authors are required to disclose any and all commercial, financial, and other relationships in any way related to the subject of this article as per ICMJE conflict of interest guidelines (see www.icmje.org). The authors have stated that no such relationships exist.

Publication dates: Received for publication November 16, 2018. Revision received December 6, 2018. Accepted for publication December 10, 2018. Available online February 4, 2019.

REFERENCES

1. Swanson ER, Seaberg DC, Mathias S. The use of propofol for sedation in the emergency department. *Acad Emerg Med.* 1996;3:234-238.
2. Miner JR, Burton JH. Clinical practice advisory: emergency department procedural sedation with propofol. *Ann Emerg Med.* 2007;50:182-187. 187.e1.
3. Godwin SA, Burton JH, Gerardo CJ, et al. Clinical policy: procedural sedation and analgesia in the emergency department. *Ann Emerg Med.* 2014;63:247-258.e18.
4. Harvey M, Cave G, Betham C. Contemporary sedation practice in a large New Zealand emergency department. *N Z Med J.* 2011;124:36-45.
5. Bell A, Taylor DM, Holdgate A, et al. Procedural sedation practices in Australian emergency departments. *Emerg Med Australas.* 2011;23:458-465.
6. Coté CJ, Wilson S; American Academy of Pediatrics; American Academy of Pediatric Dentistry. Guidelines for monitoring and

- management of pediatric patients before, during, and after sedation for diagnostic and therapeutic procedures: update 2016. *Pediatrics*. 2016;138:e1-e31.
7. Bhatt M, Kennedy RM, Osmond MH, et al. Consensus-based recommendations for standardizing terminology and reporting adverse events for emergency department procedural sedation and analgesia in children. *Ann Emerg Med*. 2009;53:426-435.e4.
 8. Green SM, Roback MG, Krauss BS, et al. Policy statement: procedural sedation in the emergency department. Available at: <https://www.acep.org/globalassets/new-pdfs/policy-statements/procedural-sedation.in.the.ed.pdf>. Accessed August 30, 2018.
 9. Miner JR, Huber D, Nichols S, et al. The effect of the assignment of a pre-sedation target level on procedural sedation using propofol. *J Emerg Med*. 2007;32:249-255.
 10. Miner JR, Biros MH, Seigel T, et al. The utility of the bispectral index in procedural sedation with propofol in the emergency department. *Acad Emerg Med*. 2005;12:190-196.
 11. Miner JR, Biros MH, Heegaard W, et al. Bispectral electroencephalographic analysis of patients undergoing procedural sedation in the emergency department. *Acad Emerg Med*. 2003;10:638-643.
 12. Miner JR, Driver BE, Moore JC, et al. Randomized clinical trial of propofol versus alfentanil for moderate procedural sedation in the emergency department. *Am J Emerg Med*. 2017;35:1451-1456.
 13. Schick A, Driver B, Moore JC, et al. Randomized clinical trial comparing procedural amnesia and respiratory depression between moderate and deep sedation with propofol in the emergency department. *Acad Emerg Med*. 2018; <https://doi.org/10.1111/acem.13548>.
 14. Asserhøj LL, Mosbech H, Krøigaard M, et al. No evidence for contraindications to the use of propofol in adults allergic to egg, soy or peanut. *Br J Anaesth*. 2016;116:77-82.
 15. Murphy A, Campbell DE, Baines D, et al. Allergic reactions to propofol in egg-allergic children. *Anesth Analg*. 2011;113:140-144.
 16. Lambert R, Frank M, Wadams H, et al. Safety of propofol sedation in children with known food allergies. *Crit Care Med*. 2011;39:234.
 17. Mehta H, Chehade M. Safety of propofol use in patients with food allergies. *J Allergy Clin Immunol*. 2014;133:AB152.
 18. Wiskin AE, Smith J, Wan SKY, et al. Propofol anaesthesia is safe in children with food allergy undergoing endoscopy. *Br J Anaesth*. 2015;115:145-146.
 19. Pongdee T. Soy-allergic and egg-allergic can receive anesthesia. Available at: <https://www.aaaai.org/conditions-and-treatments/library/allergy-library/soy-egg-anesthesia>. Accessed August 15, 2018.
 20. Cravero JP, Beach ML, Blike GT, et al. Pediatric Sedation Research Consortium. The incidence and nature of adverse events during pediatric sedation/anesthesia with propofol for procedures outside the operating room: a report from the Pediatric Sedation Research Consortium. *Anesth Analg*. 2009;108:795-804.
 21. Mallory MD, Baxter AL, Yanosky DJ, et al. Pediatric Sedation Research Consortium. Emergency physician-administered propofol sedation: a report on 25,433 sedations from the Pediatric Sedation Research Consortium. *Ann Emerg Med*. 2011;57:462-468.e1.
 22. Tobias JD, Leder M. Procedural sedation: a review of sedative agents, monitoring, and management of complications. *Saudi J Anaesth*. 2011;5:395-410.
 23. Havidich JE, Beach M, Dierdorf SF, et al. Preterm versus term children: analysis of sedation/anesthesia adverse events and longitudinal risk. *Pediatrics*. 2016;137:e20150463.
 24. Burton JH, Miner JR, Shipley ER, et al. Propofol for emergency department procedural sedation and analgesia: a tale of three centers. *Acad Emerg Med*. 2006;13:24-30.
 25. Schnider TW, Minto CF, Shafer SL, et al. The influence of age on propofol pharmacodynamics. *Anesthesiology*. 1999;90:1502-1516.
 26. Astra-Zeneca. Diprivan [package insert]. Cambridge, United Kingdom: AstraZeneca Pharmaceuticals; 2017.
 27. Kazama T, Ikeda K, Morita K, et al. Comparison of the effect-site $k(e)0s$ of propofol for blood pressure and EEG bispectral index in elderly and younger patients. *Anesthesiology*. 1999;90:1517-1527.
 28. Homfray G, Palmer A, Grimsom-Powney H, et al. Procedural sedation of elderly patients by emergency physicians: a safety analysis of 740 patients. *Br J Anaesth*. 2018;121:1236-1241.
 29. Newstead B, Bradburn S, Appelboom A, et al. Propofol for adult procedural sedation in a UK emergency department: safety profile in 1008 cases. *Br J Anaesth*. 2013;111:651-655.
 30. American Society of Anesthesiologists (ASA). ASA physical status classification system. Available at: <https://www.asahq.org/resources/clinical-information/asa-physical-status-classification-system>. Accessed August 15, 2018.
 31. Hoffman GM, Nowakowski R, Troshynski TJ, et al. Risk reduction in pediatric procedural sedation by application of an American Academy of Pediatrics/American Society of Anesthesiologists process model. *Pediatrics*. 2002;109:236-243.
 32. Miner JR, Martel ML, Meyer M, et al. Procedural sedation of critically ill patients in the emergency department. *Acad Emerg Med*. 2005;12:124-128.
 33. Rutman MS. Sedation for emergent diagnostic imaging studies in pediatric patients. *Curr Opin Pediatr*. 2009;21:306-312.
 34. Denny MA, Manson R, Della-Giustina D. Propofol and etomidate are safe for deep sedation in the emergency department. *West J Emerg Med*. 2011;12:399-403.
 35. Taylor DM, Bell A, Holdgate A, et al. Risk factors for sedation-related events during procedural sedation in the emergency department. *Emerg Med Australas*. 2011;23:466-473.
 36. Beach ML, Cohen DM, Gallagher SM, et al. Major adverse events and relationship to nil per os status in pediatric sedation/anesthesia outside the operating room: a report of the Pediatric Sedation Research Consortium. *Anesthesiology*. 2016;124:80-88.
 37. Green SM, Miner JR, Schneider S, et al. Unscheduled procedural sedation: a multidisciplinary consensus practice guideline. Available at: <https://acep.org/globalassets/sites/acep/media/policy-statement/unscheduled-procedural-sedation-sept-28-2018-cp.pdf>. Accessed October 1, 2018.
 38. Sacchetti A, Senula G, Strickland J, et al. Procedural sedation in the community emergency department: initial results of the ProSCED registry. *Acad Emerg Med*. 2007;14:41-46.
 39. Hogan K, Sacchetti A, Aman L, et al. The safety of single-physician procedural sedation in the emergency department. *Emerg Med J*. 2006;23:922-923.
 40. Vinson DR, Hoehn CL. Sedation-assisted orthopedic reduction in emergency medicine: the safety and success of a one physician/one nurse model. *West J Emerg Med*. 2013;14:47-54.
 41. Joseph CP, Vinson DR. Feasibility of single- vs two-physician procedural sedation in a small community emergency department. *Am J Emerg Med*. 2018;36:977-982.
 42. Rex DK, Heuss LT, Walker JA, et al. Trained registered nurses/endoscopy teams can administer propofol safely for endoscopy. *Gastroenterology*. 2005;129:1384-1391.
 43. Tohda G, Higashi S, Wakahara S, et al. Propofol sedation during endoscopic procedures: safe and effective administration by registered nurses supervised by endoscopists. *Endoscopy*. 2006;38:360-367.
 44. Lin D. *Sedation, Analgesia and JCAHO*. Marblehead, MA: HC Pro, Inc; 2005.
 45. Leslie K, Sessler DI, Schroeder M, et al. Propofol blood concentration and the bispectral index predict suppression of learning during propofol/epidural anesthesia in volunteers. *Anesth Analg*. 1995;81:1269-1274.
 46. Glass PS, Bloom M, Kearse L, et al. Bispectral analysis measures sedation and memory effects of propofol, midazolam, isoflurane,

- and alfentanil in healthy volunteers. *Anesthesiology*. 1997;86: 836-847.
47. Alletag MJ, Auerbach MA, Baum CR. Ketamine, propofol, and ketofol use for pediatric sedation. *Pediatr Emerg Care*. 2012;28:1391-1395; quiz 1396-1398.
 48. Khan K, Hayes I, Buggy D. Pharmacology of anaesthetic agents I: intravenous induction agents. *Contin Educ Anaesth Crit Care Pain*. 2014;14:100-105.
 49. Kaye AD, Fox CJ, Padnos IW, et al. Pharmacologic considerations of anesthetic agents in pediatric patients: a comprehensive review. *Anesthesiol Clin*. 2017;35:e73-e94.
 50. Absalom AR, Mani V, De Smet T, et al. Pharmacokinetic models for propofol—defining and illuminating the devil in the detail. *Br J Anaesth*. 2009;103:26-37.
 51. David H, Shipp J. A randomized controlled trial of ketamine/propofol versus propofol alone for emergency department procedural sedation. *Ann Emerg Med*. 2011;57:435-441.
 52. Green SM, Andolfatto G. Managing propofol-induced hypoventilation. *Ann Emerg Med*. 2015;65:57-60.
 53. Patanwala AE, Christich AC, Jasiak KD, et al. Age-related differences in propofol dosing for procedural sedation in the emergency department. *J Emerg Med*. 2013;44:823-828.
 54. Young TP, Lim JJ, Kim TY, et al. Pediatric procedural sedation with propofol using a higher initial bolus dose. *Pediatr Emerg Care*. 2014;30:689-693.
 55. Shavit I, Bar-Yaakov N, Grossman L, et al. Sedation for children with intraoral injuries in the emergency department: a case-control study. *Pediatr Emerg Care*. 2014;30:805-807.
 56. Campbell SG, MacPhee S, Butler M, et al. Emergency procedural sedation with propofol in older teenagers: any cause for concern? *Pediatr Emerg Care*. 2015;31:762-765.
 57. Barker N, Lim J, Amari E, et al. Relationship between age and spontaneous ventilation during intravenous anesthesia in children. *Pediatr Anesth*. 2007;17:948-955.
 58. West N, Dumont GA, van Heusden K, et al. Robust closed-loop control of induction and maintenance of propofol anesthesia in children. *Pediatr Anesth*. 2013;23:712-719.
 59. Ansermino JM, Magruder W, Dosani M. Spontaneous respiration during intravenous anesthesia in children. *Curr Opin Anaesthesiol*. 2009;22:383-387.
 60. Green SM, Krauss BS. Target-controlled infusions could improve the safety and efficacy of emergency department propofol sedation. *Anesth Analg*. 2016;122:283-284.
 61. Choi GJ, Kang H, Baek CW, et al. Comparison of bolus versus continuous infusion of propofol for procedural sedation: a meta-analysis. *Curr Med Res Opin*. 2017;33:1935-1943.
 62. Jenkins E, Hebban KB, Karaga KK, et al. Experience with the use of propofol for radiologic imaging in infants younger than 6 months of age. *Pediatr Radiol*. 2017;47:974-983.
 63. McFarlan CS, Anderson BJ, Short TG. The use of propofol infusions in paediatric anaesthesia: a practical guide. *Paediatr Anaesth*. 1999;9:209-216.
 64. Miner JR, Biros M, Krieg S, et al. Randomized clinical trial of propofol versus methohexital for procedural sedation during fracture and dislocation reduction in the emergency department. *Acad Emerg Med*. 2003;10:931-937.
 65. Symington L, Thakore S. A review of the use of propofol for procedural sedation in the emergency department. *Emerg Med J*. 2006;23:89-93.
 66. Weisz K, Bajaj L, Deakynne SJ, et al. Adverse events during a randomized trial of ketamine versus co-administration of ketamine and propofol for procedural sedation in a pediatric emergency department. *J Emerg Med*. 2017;53:1-9.
 67. Miner JR, Moore JC, Austad EJ, et al. Randomized, double-blinded, clinical trial of propofol, 1:1 propofol/ketamine, and 4:1 propofol/ketamine for deep procedural sedation in the emergency department. *Ann Emerg Med*. 2015;65:479-488.e2.
 68. Donnelly RF, Willman E, Andolfatto G. Stability of ketamine-propofol mixtures for procedural sedation and analgesia in the emergency department. *Can J Hosp Pharm*. 2018;61:426-430.
 69. Bedocs P, Evers DL, Buckenmaier CC. Predosing chemical stability of admixtures of propofol, ketamine, fentanyl, and remifentanyl. *Anesth Analg*. 2018; <https://doi.org/10.1213/ANE.0000000000003772>.
 70. Sharieff GQ, Trocinski DR, Kanegaye JT, et al. Ketamine-propofol combination sedation for fracture reduction in the pediatric emergency department. *Pediatr Emerg Care*. 2007;23:881-884.
 71. Willman EV, Andolfatto G. A prospective evaluation of “ketofol” (ketamine/propofol combination) for procedural sedation and analgesia in the emergency department. *Ann Emerg Med*. 2007;49:23-30.
 72. Shah A, Mosdossy G, McLeod S, et al. A blinded, randomized controlled trial to evaluate ketamine/propofol versus ketamine alone for procedural sedation in children. *Ann Emerg Med*. 2011;57: 425-433.e2.
 73. Andolfatto G, Willman E. A prospective case series of pediatric procedural sedation and analgesia in the emergency department using single-syringe ketamine-propofol combination (ketofol). *Acad Emerg Med*. 2010;17:194-201.
 74. Messenger DW, Murray HE, Dungey PE, et al. Subdissociative-dose ketamine versus fentanyl for analgesia during propofol procedural sedation: a randomized clinical trial. *Acad Emerg Med*. 2008;15:877-886.
 75. Andolfatto G, Abu-Laban RB, Zed PJ, et al. Ketamine-propofol combination (ketofol) versus propofol alone for emergency department procedural sedation and analgesia: a randomized double-blind trial. *Ann Emerg Med*. 2012;59:504-512; e1-2.
 76. Phillips W, Anderson A, Rosengreen M, et al. Propofol versus propofol/ketamine for brief painful procedures in the emergency department: clinical and bispectral index scale comparison. *J Pain Palliat Care Pharmacother*. 2010;24:349-355.
 77. Chiaretti A, Ruggiero A, Barone G, et al. Propofol/alfentanil and propofol/ketamine procedural sedation in children with acute lymphoblastic leukaemia: safety, efficacy and their correlation with pain neuromediator expression. *Eur J Cancer Care (Engl)*. 2010;19:212-220.
 78. Miner JR, Heegaard W, Plummer D. End-tidal carbon dioxide monitoring during procedural sedation. *Acad Emerg Med*. 2002;9:275-280.
 79. Hart LS, Berns SD, Houck CS, et al. The value of end-tidal CO₂ monitoring when comparing three methods of conscious sedation for children undergoing painful procedures in the emergency department. *Pediatr Emerg Care*. 1997;13:189-193.
 80. Tobias JD. End-tidal carbon dioxide monitoring during sedation with a combination of midazolam and ketamine for children undergoing painful, invasive procedures. *Pediatr Emerg Care*. 1999;15:173-175.
 81. Burton JH, Harrah JD, Germann CA, et al. Does end-tidal carbon dioxide monitoring detect respiratory events prior to current sedation monitoring practices? *Acad Emerg Med*. 2006;13:500-504.
 82. Anderson JL, Junkins E, Pribble C, et al. Capnography and depth of sedation during propofol sedation in children. *Ann Emerg Med*. 2007;49:9-13.
 83. Deitch K, Miner J, Chudnofsky CR, et al. Does end tidal CO₂ monitoring during emergency department procedural sedation and analgesia with propofol decrease the incidence of hypoxic events? a randomized, controlled trial. *Ann Emerg Med*. 2010;55:258-264.
 84. Chawla N, Boateng A, Deshpande R. Procedural sedation in the ICU and emergency department. *Curr Opin Anaesthesiol*. 2017;30: 507-512.
 85. Krauss BS, Andolfatto G, Krauss BA, et al. Characteristics of and predictors for apnea and clinical interventions during procedural sedation. *Ann Emerg Med*. 2016;68:564-573.
 86. Soto RG, Fu ES, Vila H, et al. Capnography accurately detects apnea during monitored anesthesia care. *Anesth Analg*. 2004;99:379-382; table of contents.

87. Green SM, Krauss B. Supplemental oxygen during propofol sedation: yes or no? *Ann Emerg Med.* 2008;52:9-10.
88. Patel R, Lenczyk M, Hannallah RS, et al. Age and the onset of desaturation in apnoeic children. *Can J Anaesth.* 1994;41:771-774.
89. Xue FS, Luo LK, Tong SY, et al. Study of the safe threshold of apneic period in children during anesthesia induction. *J Clin Anesth.* 1996;8:568-574.
90. Xue FS, Tong SY, Wang XL, et al. Study of the optimal duration of preoxygenation in children. *J Clin Anesth.* 1995;7:93-96.
91. Nimmagadda U, Salem MR, Crystal GJ. Preoxygenation: physiologic basis, benefits, and potential risks. *Anesth Analg.* 2017;124:507-517.
92. Kinouchi K, Tanigami H, Tashiro C, et al. Duration of apnea in anesthetized infants and children required for desaturation of hemoglobin to 95%. The influence of upper respiratory infection. *Anesthesiology.* 1992;77:1105-1107.
93. Deitch K, Chudnofsky CR, Dominici P. The utility of supplemental oxygen during emergency department procedural sedation with propofol: a randomized, controlled trial. *Ann Emerg Med.* 2008;52:1-8.
94. Lamond DW. Review article: safety profile of propofol for paediatric procedural sedation in the emergency department. *Emerg Med Australas.* 2010;22:265-286.
95. Couloures KG, Beach M, Cravero JP, et al. Impact of provider specialty on pediatric procedural sedation complication rates. *Pediatrics.* 2011;127:e1154-e1160.
96. Grunwell JR, Travers C, McCracken CE, et al. Procedural sedation outside of the operating room using ketamine in 22,645 children: a report from the Pediatric Sedation Research Consortium. *Pediatr Crit Care Med.* 2016;17:1109-1116.
97. Bhatt M, Johnson DW, Chan J, et al. Risk factors for adverse events in emergency department procedural sedation for children. *JAMA Pediatr.* 2017;171:957-964.
98. Wakai A, Blackburn C, McCabe A, et al. The use of propofol for procedural sedation in emergency departments. *Cochrane Database Syst Rev.* 2015;7:CD007399.
99. Godambe SA, Elliot V, Matheny D, et al. Comparison of propofol/fentanyl versus ketamine/midazolam for brief orthopedic procedural sedation in a pediatric emergency department. *Pediatrics.* 2003;112(1 pt 1):116-123.
100. Lameijer H, Sikkema YT, Pol A, et al. Propofol versus midazolam for procedural sedation in the emergency department: a study on efficacy and safety. *Am J Emerg Med.* 2017;35:692-696.
101. McGrane O, Hopkins G, Nielson A, et al. Procedural sedation with propofol: a retrospective review of the experiences of an emergency medicine residency program 2005 to 2010. *Am J Emerg Med.* 2012;30:706-711.
102. Zed PJ, Abu-Laban RB, Chan WWY, et al. Efficacy, safety and patient satisfaction of propofol for procedural sedation and analgesia in the emergency department: a prospective study. *CJEM.* 2007;9:421-427.
103. Ferguson I, Bell A, Treston G, et al. Propofol or ketofol for procedural sedation and analgesia in emergency medicine—the POKER study: a randomized double-blind clinical trial. *Ann Emerg Med.* 2016;68:574-582.e1.
104. Jasiak KD, Phan H, Christich AC, et al. Induction dose of propofol for pediatric patients undergoing procedural sedation in the emergency department. *Pediatr Emerg Care.* 2012;28:440-442.
105. Scheier E, Gadot C, Leiba R, et al. Sedation with the combination of ketamine and propofol in a pediatric ED: a retrospective case series analysis. *Am J Emerg Med.* 2015;33:815-817.
106. Senula G, Sacchetti A, Moore S, et al. Impact of addition of propofol to ED formulary. *Am J Emerg Med.* 2010;28:880-883.
107. Miner JR, Danahy M, Moch A, et al. Randomized clinical trial of etomidate versus propofol for procedural sedation in the emergency department. *Ann Emerg Med.* 2007;49:15-22.
108. Arora S. Combining ketamine and propofol (“ketofol”) for emergency department procedural sedation and analgesia: a review. *West J Emerg Med.* 2008;9:20-23.
109. Aouad MT, Moussa AR, Dagher CM, et al. Addition of ketamine to propofol for initiation of procedural anesthesia in children reduces propofol consumption and preserves hemodynamic stability. *Acta Anaesthesiol Scand.* 2008;52:561-565.
110. Yan JW, McLeod SL, Iansavitchene A. Ketamine-propofol versus propofol alone for procedural sedation in the emergency department: a systematic review and meta-analysis. *Acad Emerg Med.* 2015;22:1003-1013.
111. Greer A, Treston G. Factors associated with patient-reported procedural memory following emergency department procedural sedation with ketamine and propofol: a prospective cohort of 563 patients. *Emerg Med Australas.* 2018;30:200-208.
112. Tosun Z, Esmoğlu A, Coruh A. Propofol-ketamine vs propofol-fentanyl combinations for deep sedation and analgesia in pediatric patients undergoing burn dressing changes. *Paediatr Anaesth.* 2008;18:43-47.
113. Aminiahdashti H, Shafiee S, Hosseinienejad SM, et al. Propofol-fentanyl versus propofol-ketamine for procedural sedation and analgesia in patients with trauma. *Am J Emerg Med.* 2018;36:1766-1770.
114. Erden IA, Pamuk AG, Akinci SB, et al. Comparison of propofol-fentanyl with propofol-fentanyl-ketamine combination in pediatric patients undergoing interventional radiology procedures. *Paediatr Anaesth.* 2009;19:500-506.
115. Mofidi M, Rouhi R, Mahshidfar B, et al. Propofol-ketamine vs propofol-fentanyl combinations in patients undergoing closed reduction: a randomized, double-blind, clinical trial. *Adv J Emerg Med.* 2018;2:e44.
116. Rahman NHNA, Hashim A. The use of propofol for procedural sedation and analgesia in the emergency department: a comparison with midazolam. *Emerg Med J.* 2011;28:861-865.
117. Shafer SL. Advances in propofol pharmacokinetics and pharmacodynamics. *J Clin Anesth.* 1993;5(6 Suppl 1):14S-21S.
118. Bassett KE, Anderson JL, Pribble CG, et al. Propofol for procedural sedation in children in the emergency department. *Ann Emerg Med.* 2003;42:773-782.
119. Guenther E, Pribble CG, Junkins EP, et al. Propofol sedation by emergency physicians for elective pediatric outpatient procedures. *Ann Emerg Med.* 2003;42:783-791.
120. da Silva PSL, de Aguiar VE, Waisberg DR, et al. Use of ketofol for procedural sedation and analgesia in children with hematological diseases. *Pediatr Int.* 2011;53:62-67.
121. Smischney NJ, Beach ML, Loftus RW, et al. Ketamine/propofol admixture (ketofol) is associated with improved hemodynamics as an induction agent: a randomized, controlled trial. *J Trauma Acute Care Surg.* 2012;73:94-101.
122. Green SM, Andolfatto G, Krauss BS. Ketofol for procedural sedation revisited: pro and con. *Ann Emerg Med.* 2015;65:489-491.
123. Picard P, Tramèr MR. Prevention of pain on injection with propofol: a quantitative systematic review. *Anesth Analg.* 2000;90:963-969.
124. Miner JR, Bachman A, Kosman L, et al. Assessment of the onset and persistence of amnesia during procedural sedation with propofol. *Acad Emerg Med.* 2005;12:491-496.
125. Skokan EG, Pribble C, Bassett KE, et al. Use of propofol sedation in a pediatric emergency department: a prospective study. *Clin Pediatr (Phila).* 2001;40:663-671.
126. Jalota L, Kalira V, George E, et al. Prevention of pain on injection of propofol: systematic review and meta-analysis. *BMJ.* 2011;342:d1110.

127. Euasobhon P, Dej-Arkom S, Siriussawakul A, et al. Lidocaine for reducing propofol-induced pain on induction of anaesthesia in adults. *Cochrane Database Syst Rev.* 2016;2:CD007874.
128. Nathanson MH, Gajraj NM, Russell JA. Prevention of pain on injection of propofol: a comparison of lidocaine with alfentanil. *Anesth Analg.* 1996;82:469-471.
129. Green SM, Roback MG, Kennedy RM, et al. Clinical practice guideline for emergency department ketamine dissociative sedation: 2011 update. *Ann Emerg Med.* 2011;57:449-461.
130. Langston WT, Wathen JE, Roback MG, et al. Effect of ondansetron on the incidence of vomiting associated with ketamine sedation in children: a double-blind, randomized, placebo-controlled trial. *Ann Emerg Med.* 2008;52:30-34.
131. Green SM, Mason KP, Krauss BS. Pulmonary aspiration during procedural sedation: a comprehensive systematic review. *Br J Anaesth.* 2017;118:344-354.
132. Kam PCA, Cardone D. Propofol infusion syndrome. *Anaesthesia.* 2007;62:690-701.

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