

Newer pharmacologic agents for procedural sedation of children in the emergency department—etomidate and propofol

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Procedural sedation for pediatric patients having painful or anxiety-producing procedures is a necessary but often a daunting task for emergency medicine providers. This article focuses on the two agents that have most recently been described for use in this population—etomidate and propofol. Etomidate is a nonbarbiturate sedative hypnotic agent with no analgesic properties. Its rapid onset of action, short duration of action, and minimal hemodynamic effects make it an attractive agent for use in procedural sedation. Similar to previous adult studies, recent studies have shown that etomidate is both safe and effective in this pediatric population. Propofol is also a sedative hypnotic agent with rapid onset and short duration of action. Typically, it is administered as a bolus injection followed by an infusion. It has long been used for surgical procedures as well as in the intensive care unit setting, but little literature has supported its use in the pediatric emergency department. Recent studies appear to support propofol's use in this setting; however, a significant rate of side effects, including hypoxia, apnea, and decreased blood pressure, may limit its use. *Curr Opin Pediatr* 2003, 15:200–203 © 2003 Lippincott Williams & Wilkins.

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Abbreviations

RSI rapid-sequence induction

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Pediatric emergency department (ED) visits and anxiety-producing or painful procedures often go hand-in-hand. As compassionate physicians, our golden rule is to “do no harm,” but our pediatric patients and their families would prefer that our golden rule be “cause no pain.” The American College of Emergency Physicians echoes this thought in their policy statement regarding the use of pediatric sedation and analgesia in which they state that “emergency physicians should recognize children’s physical and emotional reactions to painful or threatening procedures and be prepared to offer some form of supplemental care to allay fear, assist in managing uncooperative patients, and supplement infiltrative anesthetics. Any child with significant pain should receive appropriate and adequate analgesics” [1]. Hence, research into safe and effective agents for procedural sedation has continued. Of these newer agents, etomidate and propofol are two that have recently come to the forefront (Table 1).

Etomidate

Etomidate is an imidazole, nonbarbiturate hypnotic agent that has gained increased use as an induction agent for ED intubation using rapid-sequence induction (RSI) [2,3]. Because of its rapid onset (5 to 30 seconds) and short duration (5 to 15 minutes) of action, stable hemodynamic profile, minimal respiratory depressive effects, and favorable reduction in intracranial pressure, etomidate has been safely used both as an induction agent for adult intubation and a sedative agent for adult procedural sedation. Etomidate has no analgesic properties. Its use in the pediatric population, however, has not been as well documented. In fact, because of insufficient data, the Food and Drug Administration does not currently recommend its use in children under the age of 10 years. Recent literature, however, appears to support the safety and efficacy of etomidate in the pediatric ED patient.

Etomidate has been used as a sedative agent since 1983, but because of reported adrenal insufficiency caused by either a continuous infusion or multiple dosing of etomidate, its use dramatically declined [3,4]. This adrenal dysfunction is caused by etomidate’s inhibition of the enzyme 11- β -hydroxylase that converts 11-deoxycortisol to cortisol [5]. Despite this inhibition, etomidate was found to be an excellent induction agent for RSI, with suspected minimal clinically apparent adrenal suppres-

Table 1. Quick reference to etomidate and propofol as procedural sedation agents

Drug	Type	Sedative dose	Onset of action	Duration of action	Adverse effects
Etomidate	Sedative-hypnotic	0.1–0.2 mg/kg IV	1 min	10–15 min	Oxygen desaturation, vomiting, myoclonus, pain at injection site, adrenocortical dysfunction (significant only with prolonged use)
Propofol	Sedative-hypnotic	1 mg/kg IV bolus followed by either 67–100 mcg/kg/min infusion or repeat 0.5 mg/kg boluses every 60 sec as necessary	<1 min	5–15 mins (once infusion stopped)	Oxygen desaturation, apnea, hypotension, pain at injection site, allergic reactions in patients allergic to eggs

IV, intravenous.

sion. Schenarts *et al.* [6•] completed a prospective trial measuring the serum cortisol response to exogenous cosyntropin in a small group of patients receiving etomidate for RSI. An initial decreased response to the cosyntropin stimulation test at 4 hours was found in the etomidate group but no difference was noted at 12 and 24 hours. These findings were first applied to the pediatric ED group when Sokolove *et al.* [7] retrospectively reviewed 100 pediatric patients under the age of 10 years who had been given etomidate for RSI. None of those patients required exogenous corticosteroids for presumed adrenal insufficiency. That review also showed no statistically significant decrease in patient blood pressure, again supporting the safety of etomidate for use during RSI in the pediatric age group.

As a procedural sedation agent in the ED setting, etomidate has received little attention with even less of that attention being directed to the pediatric age group. Ruth *et al.* [8••] reported a two-part feasibility study of ED patients receiving etomidate for procedural sedation. In the prospective portion of that trial, only 10 of 51 patients included were minors. The mean dose of etomidate used in all patients was 0.16 mg/kg, approximately half of the dose (0.3 mg/kg) typically used for RSI. A total of 12 complications were identified, including 5 episodes of decreased oxygen saturation, 4 episodes of myoclonus, and 1 episode each of vomiting, bradycardia, and pain on injection. All patients with oxygen desaturation responded to supplemental oxygen only. The rate of complications in the pediatric versus adult age group was not reported.

Vinson *et al.* [9••] conducted a retrospective review of 134 patients who received etomidate for ED procedural sedation, of which only 15 were between the ages of 6 and 17. The median cumulative dose was 0.19 mg/kg with 7 adverse events reported. Once again, these included oxygen desaturation, of which 80% of patients required temporary bag-valve-mask assisted ventilation as well as supplemental oxygen. Vomiting as well as one episode of second-degree heart block was also reported.

None of these complications was noted in the pediatric group.

Several studies dedicated to outpatient pediatric procedural sedation showed similar incidences of vomiting, oxygen desaturation, and myoclonus as were demonstrated in the adult studies. In particular, McDowall *et al.* [10], in a retrospective review of pediatric patients receiving etomidate before painful oncology procedures, showed a 2% incidence of oxygen desaturation, an 18% incidence of myoclonus, and a 10% incidence of vomiting. In the ED setting, Dickinson *et al.* [11••] reviewed 53 children who received etomidate for fracture or joint reduction. The mean total dose of etomidate was 0.24 mg/kg. Because of the lack of analgesic properties of etomidate, all of these children also received adjunctive opioid agents. Only three adverse events, including one episode of hypotension and tachycardia, one episode of nausea, and one required admission due to prolonged sedation, were reported. No oxygen desaturation, vomiting, or myoclonus was reported; however, because of the retrospective nature of this review, under-documentation may have occurred.

All of the previously mentioned reviews appear to support the safety of etomidate use for ED pediatric procedural sedation. Appropriate monitoring for oxygen desaturation and apnea is necessary, especially when adjunctive analgesic agents are administered [8]. Because of etomidate's lack of analgesic properties, this adjunctive opioid use is often necessary for painful procedures. Side effects, including vomiting and myoclonus, can be anticipated; however, the vomiting is self-limited and the myoclonus associated with etomidate has not been associated with electroencephalographic-confirmed seizure activity. Pretreating the patient with either fentanyl or diazepam may decrease this incidence of myoclonus [12]. Significant advantages in the use of etomidate versus other commonly used procedural sedation agents include not only the rapid onset, rapid recovery, and minimal hemodynamic effects, but also an inherent amnestic property with as many as 69% to 93% of patients

reporting complete lack of procedure recall [3,4,8••,9••]. Of course, continued research and experience with etomidate are required to fully recommend its use in pediatric procedural sedation, but the current data appear promising.

Propofol

Propofol is an agent that has long been used as an induction agent in general anesthesia as well as a sedative agent in the intensive care unit (ICU) and ambulatory surgery setting. Only recently has it been described for use as an ED procedural sedation agent. Propofol (2,6-diisopropylphenol) is a nonopioid, nonbarbiturate sedative hypnotic agent unrelated to other hypnotic agents. Similar to etomidate, propofol has a rapid onset of action (<1 minute) and rapid recovery once infusion is stopped (5 to 15 minutes). Because of these properties, it has been commonly used in general anesthesia as well as in ICU and ambulatory procedural sedation [13–16•,17•]. Its use in the pediatric ED patient, however, has not been well defined. In fact, only two articles to date address the use of propofol in this setting [18,19••].

Havel *et al.* [18] reported a prospective trial comparing midazolam with propofol for pediatric ED procedural sedation. In this study, 43 children between the ages of 2 and 18 years were given propofol as an initial bolus (1 mg/kg over 2 minutes), followed by an infusion (67–100 µg/kg/min) with additional boluses (1 mg/kg) given as required to maintain sedation. All of these patients also received morphine as an analgesic because of the lack of analgesic properties of propofol. They also all received an initial intravenous dose of lidocaine (0.5 mg/kg) to alleviate pain at the sight of propofol injection. The authors noted adequate sedation in the propofol group, as well as minimal side effects, including hypoxemia (11.6%), oversedation (32.6%), agitation (4.7%), and pain with injection (7.0%). These findings were not significantly different from the results achieved in the group receiving midazolam. Despite previously documented hypotension with propofol infusion [13], no significant hypotensive episodes were recorded. A significant decrease in total recovery time was noted, making propofol an attractive agent for use in a busy ED.

In a more recent study by Skokan *et al.* [19••], 40 pediatric ED patients between the ages of 2 months and 16 years received propofol for procedural sedation. Similar to Havel *et al.*, all patients received premedication with an opioid; however, none received lidocaine. Unlike the typical dosing regimen of a propofol bolus followed by a propofol infusion, this study used an initial bolus of 1 mg/kg followed by 0.5 mg/kg boluses up to every 60 seconds as deemed necessary by the ED physician to maintain sedation. A significant percentage of cardiopulmonary side effects were noted. This included a 30% incidence of oxygen desaturation, requiring one patient

to receive approximately 20 seconds of bag-valve-mask ventilation and prompting some of the involved physicians to routinely administer supplemental oxygen. Unlike Havel *et al.*, all patients in this study experienced a decrease in both their systolic and diastolic blood pressures; however, no evidence of decreased perfusion was noted and all hypotensive episodes resolved within 6 minutes. Of patients, 5% complained of pain at the site of injection at time of injection; however, because of the amnestic properties of propofol, none of these patients recalled the painful episode. Findings again were rapid onset of sedation and rapid recovery times.

These two studies alone do not provide sufficient evidence to support the use of propofol for ED procedural sedation in children. Significant side effects, including metabolic acidosis, apnea, bradycardia, and severe dysrhythmias, have all been previously reported with its use in the ICU setting and continued research and experience is necessary [20–23].

Conclusion

The American College of Emergency Physicians describes procedural sedation as a “technique of administering sedatives or dissociative agents with or without analgesics to induce a state that allows the patient to tolerate unpleasant procedures while maintaining cardiorespiratory function. Procedural sedation and analgesia is intended to result in a depressed level of consciousness but one that allows the patient to maintain airway control independently and continuously. Specifically, the drugs, doses and techniques used are not likely to produce a loss of protective airway reflexes” [24]. As we continue to evaluate the specific drugs, doses, and techniques that we use for pediatric ED procedural sedation, etomidate and propofol are two agents that appear to be safe and effective, thus deserving increased attention (Table 1).

References and recommended reading

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- Of outstanding interest

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