



Propofol for deep procedural sedation in the ED[☆]

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Abstract

We sought to evaluate the use of propofol (2,6-diisopropylphenol) for ED procedural sedation, particularly when administered in a routine fashion for a variety of indications.

Methods: This was a prospective observational study conducted in an urban teaching ED. Propofol was administered by handheld syringe and combined with fentanyl. Measurements included propofol and fentanyl dose, serial vital signs, pulse oximetry, adverse events, and patient and physician satisfaction.

Results: One hundred thirty-six subjects (18 to 69 years) were enrolled. Procedures included 82 (60.3%) abscess incision and drainages and 47 (34.6%) orthopedic reductions. Adverse events occurred in 14 cases (10.3%; 95% confidence interval 5.2% to 15.4%), including hypotension in 5, hypoxemia in 7, and apnea in 5. One patient required intubation. Both patient and physician satisfaction were excellent.

Conclusions: ED procedural sedation with propofol was effective and well accepted by patients and physicians. However, it produced a significant incidence of hypotension, hypoxemia, and apnea.

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1. Introduction

Patients undergoing painful procedures in the ED frequently require a potent sedative, in addition to narcotic analgesia. Propofol (2,6-diisopropylphenol) offers an alternative to other sedative agents such as midazolam, methohexital, and ketamine. Advantages of propofol include its very rapid onset of action and short duration of action as well as its antiemetic and amnestic properties.

Problems associated with propofol include apnea, hypotension, loss of protective reflexes, and a propensity to induce rapid swings between light sedation and general anesthesia. The potential danger of using propofol in the ED has been compared to driving a turbo-charged sports car, and editorialists have pointed out the need for a large prospective case series evaluating the safety and efficacy of routine propofol use by emergency physicians [1,2]. To date, there have been 8 published studies that specifically address the use of propofol in the ED setting [3-10]. Most of these studies have been conducted in children and under the closely controlled conditions of a comparative trial.

We designed a prospective observational study to evaluate the safety and efficacy of propofol for deep procedural sedation (PS) in the ED. Our primary objective

Some of the data presented here (the first 61 patients) were presented previously in poster format at the 2001 American College of Emergency Physicians Scientific Assembly, Research Forum, in Chicago.

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was to measure and record in detail the adverse reactions associated with propofol, particularly when administered by handheld syringe and used in a routine fashion for a broad range of procedures in a busy teaching ED. We sought to record and describe in detail the dose and rate of administration that was required. In addition, patient and provider satisfaction was assessed.

2. Methods

2.1. Study design

This study was a prospective observational study. The institutional review board of Alameda County Medical Center–Highland Hospital approved the study protocol.

2.2. Study setting and population

The study was performed in the ED of an urban county hospital with an annual census of 85 000. All patients ≥ 18 years requiring sedation for a painful procedure were eligible. Exclusion criteria were hypotension, a known allergy to eggs or soybeans, or pregnancy. Propofol was administered by ED attending physicians and senior residents, including but not limited to the authors of the study. These providers were asked to review and follow guidelines written at the top of every study data collection sheet but otherwise underwent no special training in the use of propofol.

2.3. Study protocol

All patients enrolled in the study underwent PS in adherence with a standard ED protocol. Intravenous (IV) access was established. Supplemental oxygen was administered via nasal cannula or bag-valve-mask (BVM). Patients were required to be NPO for 2 hours for liquids

and for 6 hours for solids. Patients underwent continuous cardiac, pulse oximetry, and automated blood pressure monitoring with resuscitation equipment at the bedside. A designated PS nurse was required to be in attendance. Providers who administered propofol were dedicated strictly to providing PS and were not involved in performing the procedure itself.

Guidelines for administration of fentanyl and propofol were written at the top of each study data sheet. It was recommended that pretreatment with fentanyl be given as a 1 to 1.5 $\mu\text{g}/\text{kg}$ bolus 1 minute before administration of propofol. Repeat fentanyl doses were given at the discretion of the provider. Propofol (10 mg/mL) was delivered by hand from a 10-mL syringe. Two 10-mL syringes were filled with propofol before beginning. It was recommended that an initial propofol bolus of 0.5 to 1.0 mg/kg be given over 30 seconds. Half the normal initial bolus dose was recommended in patients older than 65. Propofol was then infused by hand and titrated to a level of sedation deemed adequate for the procedure. The recommended technique for propofol infusion was to give 0.1 to 0.2 mg/kg as an intermittent microbolus every 30 to 60 seconds as needed. There was no recommended maximum total propofol dose.

2.4. Measurements

Medication doses, administration times, and total procedure time were recorded. Patient weights mostly were based on the patient's own estimate. All side effects and adverse reactions were recorded. Hypotension was defined as a drop in systolic blood pressure to less than 90 mm Hg. Hypoxemia was defined as oxygen saturation less than 90%. Apnea was defined as absence of spontaneous ventilation lasting 30 seconds. After the procedure, the physician providing PS was asked to rate their satisfaction with propofol as excellent, satisfactory, or unsatisfactory

Table 1 Analysis of adverse events

Age/sex	Procedure/min	Fentanyl		Propofol		Complication	Intervention	Outcome
		Bolus ($\mu\text{g}/\text{kg}$)	Total ($\mu\text{g}/\text{kg}$)	Initial bolus (mg/kg)	Titrated dose (mg/kg/min)			
18/M	Reduction/5	0.8	1.5	0.8	0.12	Apnea; desaturation 75%; emesis	BVM; intubation	Extubated after 32 min
56/M	Reduction/10	None	none	1	0.1	Desaturation 87%	AWM; 100% O ₂	Resolved
25/M	Reduction/5	1.1	1.1	1.1	0.21	Desaturation 88%	100% O ₂	Resolved
18/M	Reduction/1	1.4	1.4	1.5	0.27	Desaturation 86%	AWM; 100% O ₂	Resolved
32/F	I&D/2	2.7	2.7	1.4	0.41	Desaturation 84%	AWM; 100% O ₂	Resolved
35/M	Penis asp/5	1.1	2.2	1.1	0.11	Apnea; desaturation 80%	100% O ₂	Resolved
22/M	Reduction/5	1.4	1.4	1.4	0.14	Apnea; desaturation 89%	none	Resolved
40/M	Reduction/0.3	2.6	2.6	1	None	Apnea; no desaturation	Physical stimulation	Resolved
31/M	Reduction/4	0.7	0.7	0.9	0.43	Apnea; no desaturation	Physical stimulation	Resolved
39/M	Reduction/5	1.6	4.1	1.3	0.13	Hypotension 89/45	IVF bolus	Resolved
22/M	I&D/7	0.8	1.6	1	0.41	Hypotension 74/49	IVF bolus	Resolved
56/M	I&D/9	1.5	1.5	0.9	0.14	Hypotension 83/59	IVF bolus	Resolved
24/F	I&D/3	1.8	1.8	1.8	0.58	Hypotension 80/40	IVF bolus	Resolved
46/M	I&D/1	None	none	0.8	None	Hypotension 82/40	IVF bolus	Resolved

Abbreviations: Asp indicates aspiration; AWM, airway manipulation; BVM, bag-valve-mask ventilation; I&D, abscess incision and drainage; IVF, IV fluid.

Table 2 Comparison of medication dosage between cases associated with an adverse event and uncomplicated cases

Medication	Mean dose		Mean dose difference	P ^a
	Adverse event group (n = 14)	Uncomplicated group (n = 122)		
Fentanyl bolus	1.25 µg/kg	1.21 µg/kg	0.04 µg/kg	.428
Fentanyl total	1.61 µg/kg	2.00 µg/kg	-0.38 µg/kg ^b	.145
Propofol bolus	1.13 mg/kg	0.96 mg/kg	0.17 mg/kg	.034
Propofol infusion rate	0.26 mg/kg/min (n = 12)	0.21 mg/kg/min (n = 86)	0.04 mg/kg/min	.17

^a 1-sided T test.
^b Note the mean total fentanyl dose was higher in uncomplicated cases.

and whether they would use propofol again. Patients answered whether they remembered the procedure and whether they would receive propofol again and rated their pain as none, minimal, moderate, or severe. Study data were recorded prospectively on study data sheets by the physician providing PS and the PS nurse. Missing data were retrieved from PS nursing flow sheets.

2.5. Data analysis

Study data were entered into an Excel (Microsoft Corp, Redmond, Wash) database. Data such as medication dose, infusion rate, and procedure time were expressed as a mean and range. Measured outcomes such as adverse-event rates were expressed as a percent of total cases, accompanied by a 95% confidence interval (CI). Differences in mean medication dosage between cases with and without an adverse event were compared, and the statistical significance was determined by 1-sided *t* test. Statistical analyses were performed using SPSS statistical software (SPSS Inc, Chicago, Ill).

3. Results

Over 24 months, a total of 136 subjects were enrolled. Patient age ranged from 18 to 69 years. Procedures included 82 (60.3%) abscess incision and drainages and 47 (34.6%) orthopedic reductions. The remaining 7 were priapism aspiration, wound debridement, tube thoracostomy, diagnostic peritoneal lavage, colostomy prolapse reduction, rectal prolapse reduction, and esophagogastrroduodeno-

scopy. Average procedure time was 8.6 minutes (range 0.22-53 minutes).

The mean initial bolus dose of fentanyl was 1.2 µg/kg (range 0-3.9 µg/kg). The mean total fentanyl dose was 2.0 µg/kg (range 0-5.8 µg/kg). The mean initial bolus dose of propofol was 0.98 mg/kg (range 0.33-2.00 mg/kg). The mean propofol infusion rate (delivered by intermittent microbolus after the initial bolus dose) was 0.22 mg/kg/min (range 0.02-0.8 mg/kg/min). The mean total propofol dose was 168.6 mg (range 50-540 mg).

Adverse events occurred in a total of 14 (10.3%; 95% CI 5.2%-15.4%) cases. Hypotension occurred in 5 (3.7%; 95% CI 0.5%-6.9%) patients, hypoxemia in 7 (5.1%; 95% CI 1.4%-8.8%), and apnea in 5 (3.7%; 95% CI 0.5%-6.9%). Refer to Table 1 for details.

In a post hoc analysis, we compared the difference in medication dosage between cases in which an adverse event occurred and those without complication. The results of this analysis are summarized in Table 2. We found that, on average, the fentanyl bolus dose, initial propofol bolus dose, and propofol infusion rate were all slightly higher in the group experiencing adverse events. However, only the difference in initial propofol bolus dose was statistically significant.

Physician and patient satisfaction scores are listed in Table 3.

4. Discussion

Propofol (2,6-diisopropylphenol) is an IV sedative-hypnotic agent for use in the induction and maintenance of

Table 3 Patient and physician satisfaction

Patient questions	Response (%)					
	None	Minimal	Moderate	Severe	Yes	No
How would you rate your pain during this procedure?	66 (54.5%)	37 (30.6%)	15 (12.4%)	3 (2.5%)		
Do you remember the procedure?					14 (11.2%)	111 (88.8%)
Would you have this agent again for sedation?					118 (98.3%)	2 (1.7%)
Physician questions	Response (%)					
	Excellent	Satisfactory	Unsatisfactory	Yes	No	
How would you rate your satisfaction using propofol?	105 (81.4%)	23 (17.8%)	1 (0.8%)			
Would you use propofol again for PS?				135 (99.3%)	1 (0.7%)	

anesthesia or sedation. Propofol has many properties that make it an attractive agent for PS in the outpatient and ED setting. Propofol has a rapid onset of action, producing hypnosis usually within 40 seconds from the time of injection. Peak effect occurs at 92 seconds [11,12]. Propofol has an ultrashort half-life (distribution $t_{1/2}$ 2-4 minutes) with recovery times of within 5 to 15 minutes [11]. Propofol also has antiemetic properties and is rarely associated with emesis [1]. Disadvantages of propofol include respiratory and hemodynamic depression, narrow therapeutic window, lack of analgesic effect, and lack of a reversal agent [1,11,12].

Since its introduction in 1977 as a general anesthesia induction agent, propofol has gained popularity for PS in many settings. Its use by nonanesthesiologists has been studied and declared safe in the setting of bronchoscopy, cardioversion, percutaneous transluminal coronary angioplasty, endoscopy, and dental procedures [13-17]. To date, there have been 8 published studies specifically examining use of propofol for PS in the ED setting. The largest of these, by Bassett et al [9], involved 393 children who received propofol for brief orthopedic procedures. There have been 4 studies involving adult patients. In one study, propofol was administered by automatic pump to 20 patients [10], and in another, involving 21 patients, the dosing method was not described [6]. In a study by Coll-Vinent et al [8], propofol was administered as a single 1.5 mg/kg bolus to 9 adults undergoing electrical cardioversion. Miner et al [5] described the use of propofol, given as a 1 mg/kg bolus followed by 0.5 mg/kg every 2 minutes as needed, in 51 adult patients undergoing orthopedic procedures. In the study by Miner et al, propofol was administered in the closely controlled setting of a randomized comparative trial with methohexatol. Ours is the largest, prospective, ED study of the use of propofol for PS in adults. We sought to measure and characterize adverse events during PS with propofol, particularly when used in a routine fashion in a busy academic ED.

Hypotension is a known dose-dependent complication of propofol that appears to be caused by both vasodilation and myocardial depression. In our study, hypotension occurred in 5 patients (3.7%). (Refer to Table 1 for details.) This was transient, lasting less than 1 minute in every case, yet clinically significant in that it required an IV fluid bolus in each case. Whereas some prior ED propofol studies have reported no significant hypotension [5,8], others found a similar incidence of transient hypotension to our study. In the report by Swanson et al [10], 1 of 20 adults (5%) had a fall in systolic blood pressure to 80 mm Hg that resolved spontaneously by the next blood pressure measurement. Skokan et al [4] found that systolic and diastolic blood pressure fell in all 40 children receiving propofol, requiring fluid bolus in 2. Similarly, Bassett et al [9] found that, among 393 pediatric cases, blood pressure fell transiently in 92% (mean systolic decrease 10 mm Hg). Taken together with these other reports, our findings point out the importance of limiting use of propofol to patients with normal baseline blood pressure and robust cardiovascular reserve.

Respiratory depression from propofol, leading to apnea and/or hypoxemia, appears to be related to dose and rate of administration, as well as to concomitant use of other medications [11,12]. In one ED study, respiratory depression, as detected by end-tidal CO₂ monitoring, occurred in 45% of adults receiving propofol [5]. Hypoxemia (oxygen saturation <90%) was reported to occur in 5% to 44% of patients in prior ED studies [3,4,8-10], although routine use of supplemental oxygen varied. In our study, despite supplemental oxygen, 7 (5.1%) patients experienced hypoxemia, and in 3 cases, this was associated with apnea. One patient, described in detail below, required BVM ventilation followed by endotracheal intubation. In the other 6 patients, hypoxemia was transient and resolved with physical stimulation, airway manipulation (usually jaw thrust), and delivery of high-flow oxygen by facemask.

In our study, 5 (3.7%) patients experienced apnea lasting more than 30 seconds, 3 of whom became hypoxemic. One patient was intubated. Four patients recovered, either spontaneously or after physical stimulation, and none of these required BVM-assisted ventilation. Swanson et al reported that 2 (10%) of 20 adult patients experienced transient apnea, 1 requiring BVM ventilation [10]. In the study by Miner et al, 2 (4%) patients in the propofol arm required BVM for apnea, whereas in the study by Coll-Vinent et al [8], 2 (22%) of 9 adults receiving a single 1.5 mg/kg bolus of propofol required BVM for apnea. Clearly, respiratory depression requiring immediate intervention is the predominant complication of ED PS with propofol.

Emesis rarely complicates the use of propofol, probably because of its antiemetic property. In our study, 1 patient experienced emesis with no evidence of aspiration. This patient was intubated. In prior ED studies, there were no reported episodes of emesis [3-10].

Ours is the only ED study of propofol for PS in which a subject required intubation. The patient was an 18-year-old man with a history of mild asthma who underwent PS for reduction of a distal radius fracture. During PS, he developed prolonged apnea, hypoxemia (nadir SpO₂ 75%) and emesis. Bag-valve-mask ventilation was attempted, succinyl choline was administered, and the patient was orally intubated. The patient was extubated in 32 minutes without evidence of adverse sequelae. The development of prolonged apnea at the time of PS was likely related to medications that were given before PS. In the 95 minutes before PS, he received 8 mg of morphine IV and 2 mg of lorazepam IV, as well as immediate premedication with 0.8 mg/kg of fentanyl. The total dose of fentanyl and propofol used and the rate of propofol infusion were similar to the study mean. Refer to Table 1 for details.

An iatrogenic narcotic overdose likely occurred, but lorazepam may have also contributed. In one study that examined the synergistic effects of propofol and benzodiazepines, the dose of propofol required to produce anesthesia was reduced by 52% in the presence of midazolam [18]. Laryngospasm is another possible explanation for this

patient's course. Laryngospasm is a known complication of propofol that occurs with a frequency of less than 1% [12]. This is a consideration because the provider managing the patient's airway noted that BVM ventilation was very difficult despite an oral airway being in place and the absence of wheezes. The ventilation difficulty resolved after administration of a paralytic. A third, less likely explanation for this patient's course is fentanyl-associated rigid chest syndrome.

We chose to administer propofol from a handheld syringe. The initial propofol bolus averaged 0.98 mg/kg. This was followed by intermittent microboluses of 10 to 20 mg based on estimated patient weight, every 30 to 60 seconds, titrated to level of sedation. The mean microbolus infusion rate was 0.22 mg/kg/min (about 14 mg every minute in a 70-kg adult). For procedures lasting greater than 2 to 3 minutes, additional microboluses were usually required when purposeful movement resumed. While explicit dosing guidelines were recommended, dosing parameters were not actually controlled. Consequently, we found that microbolus infusion rates varied substantially, with a range of 0.02 to 0.8 mg/kg/min (from about 1.5 to 55 mg/min for a 70-kg adult).

In contrast to our dosing protocol, early ED studies of propofol for PS delivered propofol by continuous IV infusion, using a pump [3,10]. The slow continuous infusion technique suffers from a longer feedback loop between perceived level of sedation and adjustment of infusion rate. Thus, it is prone to produce undersedation or oversedation. A nurse usually operates the IV pump. The intermittent microbolus technique likely results in tighter control of the level of sedation and requires less nursing involvement. Its main disadvantage is that there is no direct limit on the rate of infusion, and overdose may be more likely to occur by accident or if the anesthetist is impatient.

Whereas 6 prior ED studies appear to have used a similar propofol dosing method to ours, in none of these was dosing precisely described or measured. One study which used a higher bolus dose of 1.5 mg/kg found a very high rate of both hypoxemia (44%) and apnea (22%) [8]. In the large pediatric series by Bassett et al [9], a 1 mg/kg bolus was followed by subsequent doses of 0.5 mg/kg infused over 60 seconds, every 1 to 2 minutes. The study in adults by Miner et al [5] used a similar regimen of a 1 mg/kg initial bolus, followed by 0.5 mg/kg every 3 to 5 minutes. These regimens, in which larger subsequent boluses were administered more slowly and less frequently than in our "microbolus" protocol, produced similar rates of hypoxia and apnea to those in our study.

In our study, physician and patient satisfaction was assessed using descriptive ratings. Please refer to Table 3 for details. We chose not to use a visual analog scale because no comparison was being made. Descriptive ratings were felt to be more meaningful in this setting. In the 129 cases where satisfaction was recorded, physicians rated satisfaction with propofol as 'excellent' in 105 (83.2%; 95% CI 74.7%-

88.1%). In the 24 cases where physician satisfaction was rated less than excellent, dissatisfaction was noted to be caused by 1 or more of the following: difficulty achieving adequate sedation, excess patient movement, and occurrence of apnea or hypoxemia. Physicians stated they would use propofol again in all but one case.

Patient satisfaction was similarly excellent. Eighty nine percent (95% CI 83.3%-94.3%) of patients did not remember the procedure, and 98.3% stated that they would be willing to receive propofol again. However, 15% (95% CI 8.5-21.2%) of patients rated pain during the procedure as moderate or severe. This finding underscores the need to provide adequate doses of an analgesic agent when using propofol for PS.

Although our study was not explicitly designed to do so, we compared medication dosage between cases associated with adverse events and uncomplicated cases. We found that the propofol bolus dose was significantly higher in the adverse-event group and that there was a trend toward higher propofol infusion rate and initial fentanyl bolus dose. This association between adverse events, such as apnea, and higher propofol and fentanyl dosage is very plausible and likely to be true. Furthermore, close analysis of the single case requiring intubation suggests that benzodiazepines and narcotics may potentiate the respiratory depression from propofol.

Our study suffers from a number of shortcomings. The most significant problems were a wide variation in PS conditions throughout the study and failure to obtain certain data that are considered standard in sedation studies. In an effort to promote the use of propofol by many providers under routine conditions, we purposefully designed a loose study protocol and a brief data collection sheet that focused strictly on dosing, complications, and satisfaction. We did not use research assistants. The trade-off was that we did not closely control study conditions or provider behavior and were unable to gather detailed information on each case. We did not quantify recovery time, although the very short recovery time after sedation with propofol has been firmly established in other studies [8,9]. American Society of Anesthesiology class was not formally assessed and recorded, although patients with abnormal hemodynamics or active cardiopulmonary problems were not considered for PS with propofol. We did not quantify the level of training or prior experience with propofol of the physician providing PS.

In the process of conducting this study, we realized that there were shortcomings in our propofol PS guidelines. Foremost was the lack of required end-tidal CO₂ monitoring. Continuous capnography during PS is rapidly becoming standard of care because it is known to detect respiratory depression earlier than physical examination or pulse oximetry [6]. Its routine use during this study might have reduced the incidence of hypoxemia. Second, our PS guidelines should have prompted providers to carefully consider other medications that the patient may have received before PS. In patients receiving benzodiazepines

or narcotics before PS, the propofol dose should be reduced or the procedure delayed.

In conclusion, propofol was effective for deep PS in the ED, when used in a routine fashion for a variety of indications. Physician and patient satisfaction with this form of PS was excellent. However, there was a significant incidence of hypotension, hypoxemia, and apnea, and 1 of 136 patients required intubation. Adverse events were associated with a higher initial bolus dose of propofol. Careful patient selection and scrupulous monitoring during PS with propofol are mandatory.

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