Procedural Sedation of Critically Ill Patients in the Emergency Department

James R. Miner, MD, Marc L. Martel, MD, Madeline Meyer, MD, Robert Reardon, MD, Michelle H. Biros, MS, MD

Abstract

Objectives: Procedural sedation is routinely performed in the emergency department (ED). However, some authors believe it is unsafe in nonintubated, critically ill patients. The objective of this study was to determine the safety of ED procedural sedation in the American Society of Anesthesiologists (ASA) physical status classification P3 and P4 patients. **Methods:** This was a prospective observational study of patients undergoing procedural sedation in the ED between August 2002 and December 2003 who were classified as ASA physical status score P3 or P4. Patients received either propofol or etomidate at the discretion of the treating physician before their painful procedure. Doses, vital signs, end-tidal CO_2 ($ETCO_2$) by nasal cannulae, and pulse oximetry were recorded. Respiratory depression (RD) was defined as a change from baseline $ETCO_2$ >10 mm Hg, an oxygen saturation of <90%, or an absent $ETCO_2$ waveform at any time. **Results:** Sixty-two critically ill, nonintubated patients were enrolled. Thirty-one patients received propofol, and 31 patients received etomidate. No cardiac rhythm abnormalities were detected. RD was seen in 37 of 62 patients (59.7%): 19 of the 31 (61.3%) who received propofol and 18 of the 31 (58.1%) who received etomidate. The mean decrease from baseline systolic blood pressure was 11.3% (95% confidence interval [CI] = 7.3% to 15.5%): 5.0% (95% CI = 3.0% to 8.1%) for those receiving etomidate and 17.1% (95% CI = 9.9% to 24.3%) for those receiving propofol. No adverse events were reported. **Conclusions:** The rate of subclinical RD detected by these criteria was similar to previous reports for noncritically ill patients. Procedural sedation of nonintubated ASA physical status score P3 and P4 patients in the ED with either propofol or etomidate appears to be safe.

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When procedural sedation for painful procedures is performed in the emergency department (ED), several unique challenges are encountered. Because it is not possible to predict when these procedures will be necessary, it is difficult to plan ahead for their implementation. These procedures are seldom elective in the ED setting; patient selection cannot be done to isolate the procedures with optimal chances of a perfect outcome at a time that is convenient for the patient and the physician.

The patients in whom this difficulty is most pronounced are those who are acutely critically ill. Often, when a critically injured patient arrives in the ED, the patient is in pain or requires a rapid and brief painful procedure, such as fracture reduction, chest tube placement, or cardioversion. When critically ill patients require endotracheal intubation, sedation and pain control are straightforward. There is, however, a subset of critically ill patients who do not necessarily require intubation but who do need a brief painful procedure to manage their acute illness or injury. By using moderate and deep procedural sedation in this group, intubation can sometimes be avoided. On the other hand, patients who are critically injured may be at risk of complications from the use of sedatives, such as hypotension or respiratory depression (RD). The emergency physician may therefore hesitate to use or avoid the use of sedatives and attempt to perform the painful procedure with no or minimal sedation. While some may consider this to be safest in critically injured or ill patients, failing to adequately treat pain is unlikely to improve the patient's outcome.

The American Society of Anesthesiologists (ASA) physical status classification system was developed to classify the illness of patients before sedation (Table 1).[1] Procedural sedation in the ED is usually performed and has been most extensively evaluated in patients who are classified as P1 or P2, and the rate of adverse events in these groups has been found to be low.[2] There are critically ill ED patients (ASA class of P3 or greater) who require sedation. The safety of sedation in these ED patients has not been extensively studied. Green et al.[3] studied safety issues in critically ill pediatric ED patients receiving sedation with ketamine, but information concerning critically ill adults

From the Department of Emergency Medicine, Hennepin County Medical Center (JRM, MLM, MM, RR, MHB), Minneapolis, MN.
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Address for correspondence and reprints: James R. Miner MD, Department of Emergency Medicine, Hennepin County Medical Center, 701 Park Avenue South, Minneapolis, MN 55415. Fax: 612-904-4241; e-mail: miner015@umn.edu.
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TABLE 1. American Society of Anesthesiologists Physical Status Classification System[1]

P1	A normal healthy patient
P2	A patient with mild systemic disease
P3	A patient with severe systemic disease
P4	A patient with severe systemic disease that is a constant threat to life
P5	A moribund patient who is not expected to survive without the operation
P6	A declared brain-dead patient whose organs are being removed for donor purposes

who are not intubated before sedation for procedures is sparse.

Critically ill patients who are not endotracheally intubated sometimes require pain management with procedural sedation but may be at a higher risk of the adverse effects of sedative medicines, such as RD or hypotension, than less critically ill patients. Etomidate and propofol have been evaluated in more stable ED patients with a low rate of these adverse events.[4–7] The goal of this study was to prospectively analyze the safety of ED procedural sedation of critically ill adult patients in the ED receiving either propofol or etomidate by comparing the rate of RD, active airway interventions, hypotension, and other complications with previous reports concerning the procedural sedation of more stable ED patients.

METHODS

Study Design. This was a prospective observational study of adult ED patients undergoing procedural sedation with etomidate or propofol. The institutional review board of Hennepin County Medical Center approved the study. This study used data from noninvasive monitors that were part of the usual care of critically ill patients undergoing procedural sedation. The institutional review board therefore deemed consent before enrollment unnecessary, because the study entailed no additional risk to the patients and did not drive patient management.

Study Setting and Population. This study was performed at Hennepin County Medical Center, an urban county hospital with approximately 93,000 patient ED visits per year. All adult (aged 18 years of older) ED patients undergoing treatment in the resuscitation area of the ED who were going to receive procedural sedation for a painful procedure and who had an ASA physical status score of P3 or greater were eligible for study enrollment. Patients were enrolled between August 1, 2002, and December 31, 2003. Patients were excluded if they had a known hypersensitivity to either medication, were pregnant, or had clinical evidence of intoxication before the start of the procedure. In our ED, procedural sedation is performed at the discretion of the treating emergency physician. It is the standard of care in our ED to treat critically injured patients who are awake and in pain with intravenous fentanyl (1 μg/kg intravenously followed by 0.5 μg/kg intravenously every 5 minutes as needed/tolerated) for pain control as soon as possible upon their arrival.

Study Protocol. All patients were placed on cardiac, blood pressure, pulse oximeter, and nasal sample end-tidal CO_2 ($ETCO_2$) monitors, as per standard guidelines for procedural sedation and critical care in our ED. Data were collected by trained research assistants. All patients received supplemental oxygen. During the procedure, the patient was monitored by one physician, while another physician performed the procedure. Baseline values were recorded. During the procedure, agents used and doses were recorded. Furthermore, pulse oximetry, heart rate, blood pressure, respiratory rate, and $ETCO_2$ were monitored continuously and recorded every minute. Any loss of $ETCO_2$ waveform or the use of airway adjuncts, such as bag-valve-mask–assisted respirations or oral airway placement, was also noted.

Measurements. RD was defined as an oxygen saturation of <90%, a change from baseline $ETCO_2$ of >10 mm Hg, or airway obstruction with cessation of gas exchange at any time (noted by an absent $ETCO_2$ waveform).[8] After the procedure, the physician noted any complications, including, but not limited to, vomiting or aspiration, intubation, hypotension (defined as a decrease in systolic blood pressure >20%), arrhythmias, and whether or not the patient required assisted ventilations (by bag-valve mask) due to decreased protective airway reflexes during the procedure. The end point of sedation was considered the time at which the patient had regained his or her baseline mental status.

Data Analysis. Data were collected by a designated research assistant during the procedure and were then entered into an Excel (Microsoft Corp., Redmond, WA) database for further analysis. All analysis and interpretation of data was performed using Stata (Stata Corp., College Station, TX) statistical software. Data were analyzed using descriptive statistics.

RESULTS

Sixty-two patients were enrolled in the study, with a mean age of 34.0 years (95% confidence interval [CI] = 30.4 to 37.7). Fifteen of 62 (24.2%) were ASA physical status P3, and 48 of 62 (75.8%) were P4. Thirty-one patients received etomidate, and 31 received propofol. The mean initial dose for patients receiving etomidate was 0.25 mg/kg (95% CI = 0.17 to 0.34), and the mean total dose was 0.40 mg/kg (95% CI = 0.26 to 0.53). The mean initial dose for patients

receiving propofol was 0.96 mg/kg (95% CI = 0.84 to 1.10), and the mean total dose was 1.80 mg/kg (95% CI = 1.41 to 2.19).

Respiratory depression was seen in 37 of 62 patients (59.7%): 18 of 31 (58.1%) who received etomidate and 19 of 31 (61.3%) who received propofol. The individual criteria for RD by agent received are presented in Table 2. The mean initial $ETCO_2$ value was 35.5 mm Hg (95% CI = 32.4 to 38.5), and the mean change from baseline $ETCO_2$ to the nadir was 10.9 mm Hg (95% CI = 8.5 to 13.4). All patients who met the criteria for RD had a change from baseline $ETCO_2$ >10 mm Hg. The mean initial oxygen saturation was 98.9% (95% CI = 98.5% to 99.4%), and the mean lowest oxygen saturation recorded was 95.9% (95% CI = 94.5% to 97.5%). No patient experienced an absent $ETCO_2$ waveform or an oxygen saturation <90% for more than one minute. Of the three patients with an oxygen saturation <90% at some time, the lowest recorded values were 61%, 81%, and 86%. The patient whose oxygen saturation decreased to 61% had received 0.3 mg/kg of etomidate in two equal doses of 0.15 mg/kg two minutes apart. This patient received bag-valve-mask ventilation and had an oxygen saturation of 100% within one minute. The other two patients had received propofol, with the first receiving a 1-mg/kg bolus followed by a 0.5-mg/kg dose two minutes later and the second receiving a 1-mg/kg bolus followed by three 0.5-mg/kg doses, each two minutes apart. Five patients required bag-valve-mask ventilation at some point during the procedure: four of 31 of those who received etomidate and one of 31 who received propofol.

The mean initial systolic blood pressure was 136.1 mm Hg (95% CI = 130.8 to 141.3), and the mean lowest systolic blood pressure recorded was 121.3 mm Hg (95% CI = 116.8 to 125.8). The mean decrease in systolic blood pressure from baseline to nadir during the procedure was 11.3% (95% CI = 7.3% to 15.5%), for patients receiving etomidate it was 5.54% (95% CI = 3.00 to 8.10), and for patients receiving propofol it was 17.1% (95% CI = 9.9 to 24.3). Nine patients had a decrease in systolic blood pressure >20%: one of 31 who received etomidate and eight of 31 who received propofol. The mean decrease for this group was 31.4% (95% CI = 26.0% to 36.8%; range, 21%–39%). No cardiac arrhythmias or vomiting were noted during or immediately after these sedations, and no patient required subsequent intubation.

TABLE 2. Respiratory Depression Criteria

	Etomidate (*n*)	Propofol (*n*)	Total (*n*)	p-value
Oxygen saturation <90%	1	2	3	0.55
Absent $ETCO_2$ waveform	13	8	41	0.18
Change in $ETCO_2$ >10 mm Hg	18	19	36	1.00

Procedures completed included 12 (19.3%) cardioversions, 15 (24.2%) thoracostomy tube placements, and 36 (58.1%) fracture or dislocation reductions. All but four of 62 of the procedures were successful; all of the unsuccessful procedures were fracture/dislocation reductions in patients who had received etomidate. The mean time to return of baseline mental status was 10.3 minutes (95% CI = 8.9 to 11.8): 11.8 minutes (95% CI = 9.7 to 13.9) for patients receiving etomidate and 8.8 minutes (95% CI = 6.8 to 10.7) for patients receiving propofol.

DISCUSSION

To the best of our knowledge, procedural sedation of nonintubated critically ill patients in the ED has had limited evaluation. In this study, we found that the sedation of patients with an ASA physical assessment classification of P3 and P4 undergoing resuscitation in the ED appears to be safe. The need for bag-valve-mask ventilation was similar for propofol,[4,7] and the rate of hypoxia detected was lower than what has been recently reported for noncritically ill patients for etomidate[6] and for propofol.[4] The doses used here were similar to those that have typically been described for these two agents. Although there are little data to describe the minimum dose of these agents required to induce adequate sedation, the doses used in this study are close to what has been described in previous studies of ED procedural sedation.[4–6,9–11] We observed some differences in the two agents used, including changes in blood pressure, time of the procedure, and procedural success. It appears that using either etomidate or propofol for the sedation of critically ill patients has rates of complications similar to previous reports for both agents in more stable patients.

The rate of RD we found was slightly higher than our previous studies for propofol using the same criteria[4,7] and was similar between the two agents used in this study. We have previously used this definition as a marker of patients at risk for clinically significant RD. All patients who experienced a loss of $ETCO_2$ waveform had a change in $ETCO_2$ from baseline >10 mm Hg. We have, in our previous studies, observed a higher percentage of patients experiencing hypoxia. All of the patients in the current study received supplemental oxygen, and it is likely that hypoxia was not seen as often as the other signs of RD due to the high oxygen saturation in patients on supplemental oxygen. In this study, the $ETCO_2$, both in terms of change from baseline and in loss of waveform, appears to be a more sensitive detector of impending RD than oxygen saturation. Because these agents are titratable, information indicating impending respiratory compromise before clinically significant RD occurring is very useful before the administration of the next bolus of medicine. The use of decreasing oxygen saturation as the sign of impending

RD in this study would have only detected three patients at risk. On the other hand, 41 patients were observed to have a loss of $ETCO_2$ waveform, indicating a cessation of gas exchange, and 38 of these patients did not exhibit low oxygen saturation. This suggests that the supplemental oxygen decreased hypoxia in the face of hypoventilation and that oxygen saturation alone did not detect impending RD.

The primary difference between the rates of RD we found here and those in our previous reports is the number of patients who experienced loss of $ETCO_2$ waveform. This loss of waveform indicates a cessation of gas exchange and therefore represents an apneic period. The higher proportion of RD patients with this finding suggests that these patients had actually experienced more severe RD than patients in previous reports, but it was otherwise masked by supplemental oxygen.

The criteria used for RD were not intended to detect patients who have experienced actual airway compromise but rather to detect patients with subtle changes in their breathing patterns associated with RD. Although it is associated with complications, RD is an expected effect of the sedatives used in this study. The criteria are intended to detect hypoxia, brief apnea (as detected by a loss of $ETCO_2$ waveform), hypercapnia, hypoventilation (decreasing $ETCO_2$ values due to increased proportion of room air), and airway obstruction (decreasing $ETCO_2$ values due to increased mixing with room air). These changes do not represent patients who are having a complication, but rather those who are beginning to experience some of the negative respiratory effects of the sedative agent. We observed a slightly higher rate of RD than had been seen in previous reports, with a similar rate of active airway interventions by the treating physician.

Several patients experienced a decrease in systolic blood pressure. All but one of the patients who experienced hypotension had received propofol. While slight temporary hypotension may not be clinically significant in patients who are not critically ill, patients with ASA physical status scores P3 and P4 may not tolerate further decreases in blood pressure due to medications. The decrease in blood pressure we observed among patients receiving propofol is more pronounced than in previous reports.[4,12] It may be that in critically ill patients the capacity to compensate for the cardiodepressive effects of propofol is diminished.

While both of these agents appear safe, there may be different roles for each. Propofol may provide a shorter time of sedation, and etomidate may cause less hypotension. In some patients or with some procedures, it is possible that these observations may direct the choice of sedation agent. Despite the fact that all of these patients were allowed nothing by mouth and all had arrived in the ED for emergent treatment, there was no vomiting associated with procedural sedation. While 62 patients is not enough to make conclusions about the risk of an infrequent complication such as aspiration associated with procedural sedation, it is reassuring that vomiting was not an issue in this patient population of critically ill or injured patients in need of a brief painful procedure.

LIMITATIONS

We made no attempt to randomize the agents and did not compare them. We believed that consent before enrollment would be necessary before randomizing the agents and that consent would be inappropriate in critically ill patients. Both agents are used extensively in our department. An equal number of patients received each medication. We had intended to enroll 60 patients in the study and had 62 when enrollment concluded, and the equal number receiving each medication was coincidental.

A randomized trial comparing these two agents will be necessary to determine if there is a difference in their safety. Due to the design of this study, we can only conclude that neither agent was associated with a higher rate of complications than had been found in previous reports of procedural sedation done in less critically ill patients.

The term ''critically ill'' as we have used it here is loosely defined. Patients included in the study were undergoing treatment in the resuscitation area of our ED. We have no criteria for placing patients in the resuscitation area of the ED other than the emergency physician believed the patient needed resuscitation. The ASA classification was added as an additional inclusion criterion in order to better define these patients.

Establishing the safety of ED procedural sedation has been a challenge to all studies on the subject. The rate of complications is low, and there is little consensus among various reports as to what constitutes an adverse event or complication. We incorporated RD criteria as surrogate markers to show patients who were at risk of complications in order to more sensitively detect patients developing negative effects of the sedatives. A much larger study would be preferable, but in light of the paucity of data on the subject of procedural sedation of critically injured patients, and the fact that several thousand patients will be needed to establish the complication rate conclusively, we believe that smaller studies such as this are of value to the progression of research in this area. This study represents our attempt to establish a starting point for future evaluations. Baseline rates of complications and active airway interventions have been described in observation studies of sedation in stable patients, and we compared these with our RD criteria in previous studies of the subject. We cannot attempt to classify what an acceptable rate of complications is, only that the rate of RD and complications

here are similar to previous reports of the sedation of ASA physical status classification P1 and P2 patients, which is generally regarded as acceptable.

CONCLUSIONS

The rates of RD, hypotension, and active airway interventions for these critically ill or injured patients are similar to previous reports for ED procedural sedation of patients who are not critically ill. We saw a higher rate of hypotension than has previously been described. Procedural sedation in patients undergoing resuscitation who have an ASA physical status classification of P3 or P4 appears to be safe.

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