Does End Tidal CO$_2$ Monitoring During Emergency Department Procedural Sedation and Analgesia With Propofol Decrease the Incidence of Hypoxic Events? A Randomized, Controlled Trial

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**Study objective:** We determine whether the use of capnography is associated with a decreased incidence of hypoxic events than standard monitoring alone during emergency department (ED) sedation with propofol.

**Methods:** Adults underwent ED propofol sedation with standard monitoring (pulse oximetry, cardiac and blood pressure) and capnography and were randomized into a group in which treating physicians had access to the capnography and a blinded group in which they did not. All patients received supplemental oxygen (3 L/minute) and opioids greater than 30 minutes before. Propofol was dosed at 1.0 mg/kg, followed by 0.5 mg/kg as needed. Capnographic and SpO$_2$ data were recorded electronically every 5 seconds. Hypoxia was defined as SpO$_2$ less than 93%; respiratory depression, as end tidal CO$_2$ (ETCO$_2$) greater than 50 mm Hg, ETCO$_2$ change from baseline of 10%, or loss of the waveform.

**Results:** One hundred thirty-two subjects were evaluated and included in the final analysis. We observed hypoxia in 17 of 68 (25%) subjects with capnography and 27 of 64 (42%) with blinded capnography ($P = .035$; difference 17%; 95% confidence interval 1.3% to 33%). Capnography identified all cases of hypoxia before onset (sensitivity 100%; specificity 64%), with the median time from capnographic evidence of respiratory depression to hypoxia 60 seconds (range 5 to 240 seconds).

**Conclusion:** In adults receiving ED propofol sedation, the addition of capnography to standard monitoring reduced hypoxia and provided advance warning for all hypoxic events. [Ann Emerg Med. 2010;55:258-264.]

Please see page 259 for the Editor’s Capsule Summary of this article.
ventilatory status. Whether physicians can use capnography to decrease sedation-associated hypoxia remains unclear.

**Importance**

Although pulse oximetry, pulse rate, and blood pressure monitoring are considered routine practice during ED procedural sedation and analgesia, capnography is not. If the addition of capnography helps physicians reduces hypoxia, then perhaps it should also be routine.

**Goal of This Investigation**

We determine whether physician use of real-time capnography is associated with a 15% decrease in the incidence of hypoxia compared with standard monitoring alone during ED procedural sedation with propofol.

**MATERIALS AND METHODS**

**Study Design**

This is a prospective, randomized controlled trial conducted from November 2006 to February 2008. The institutional review board approved the study.

**Setting and Selection of Participants**

The study was conducted at Albert Einstein Medical Center, a 600-bed teaching hospital located in Philadelphia, PA, with an annual ED census of 75,000 patients.

We attempted to enroll consecutive (24 hours a day, 7 days a week) adults older than 18 years and selected for propofol sedation in accordance with our usual practice. Patients were excluded if they had severe chronic obstructive pulmonary disease; chronic oxygen requirements; hemodynamic instability; respiratory distress; pregnancy; inability to provide informed consent; allergy to propofol, morphine, or fentanyl (or other components of its formulation); or if, in the judgment of the attending emergency physician, procedural sedation could compromise patient safety. Informed consent was obtained from each subject.

Patients were randomly assigned to the study group (standard monitoring and capnography) or control group (standard monitoring and blinded capnography) by research associates using a computer-generated randomization list. Research associates and treating physicians were blinded to the randomization choice until after enrollment.

The ED staff had standard electronic monitoring (pulse oximetry, pulse rate, and blood pressure) available to them at all times. We also attached a Capnostream 20 monitor (Oridion Medical, Needham, MA), using a nasal-oral CO2 cannula capable of delivering compressed gases, with an oral sampling port to accommodate mouth breathers (Smart Capnoline O2; Oridion Medical). The Capnostream 20 monitor displays oximetry and CO2 waveform and calculates ETCO2. All patients had capnography; for the blinded (control) group, the monitor screen was adjusted to permit visualization only by the research associate.

All patients received supplemental oxygen at 3 L/minute by cannula. If the treating physician wished to deliver additional oxygen during the sedation, a nonrebreather mask connected to wall oxygen at 15 L/minute was placed over the cannula.

All patients received 0.5 μg/kg of fentanyl or 0.05 mg/kg of morphine for analgesia no fewer than 30 minutes before the administration of propofol for sedation. We started with propofol 1 mg/kg, administering additional boluses of 0.5 mg/kg until the desired level of sedation was achieved. All medication doses were calculated with ideal body weight. Patients were closely monitored from the initiation of sedation until they were back to their baseline alertness and were ready for discharge.

**Data Collection and Processing**

All data were collected by trained research associates, physicians who had participated in previous sedation studies and had no duties other than patient enrollment and data recording. They were trained in procedural sedation and analgesia, the study protocol and its definitions, all monitoring devices, and signs of respiratory depression.

They recorded age, sex, medical history, medications, allergies, types of procedures performed, vital signs, and sedation and procedure times on a standardized data collection instrument. The patient’s level of alertness was assessed at baseline, 90 seconds after preprocedure drug administration, and before discharge, using a modified Ramsay scale, a
previously validated scoring system for procedural sedation and analgesia.11-13

Before the study, we trained our physicians and nurses in the identification of respiratory depression with capnography and attached a laminated interpretation card to the monitor as a reminder. Treating physicians were instructed to perform procedural sedation and analgesia according to our standard ED protocol and that any intervention for an adverse event should be based on their judgment and clinical expertise with or without capnography, depending on randomization arm.

The Capnostream 20 records data electronically every 5 seconds during the course of each sedation, and research associates used electronic marking and time stamping to record specific events such as drug administration, beginning and end of procedure, and point of readiness for discharge. They also noted the time and nature of any intervention for respiratory depression or hypoxia, such as verbal or physical stimulation, airway realignment, use of additional oxygen, and the use of airway adjuncts, assisted ventilation, or intubation. Research associates manually recorded other sedation-associated adverse events, including hypotension, bradycardia, arrhythmia, vomiting, prolonged ED stay, or admission.

### Outcome Measures

Electronic data from each sedation were downloaded from the monitor into a Microsoft Excel 2000 (Microsoft, Redmond, WA) database and were checked for any discrepancies, with handwritten notations taken by the research associates. A printed time evaluation graph of the patient’s sedation was then produced (example in Figure 1), with the x axis showing time and the y axis depicting ETCO2, SpO2, respiratory rate, and pulse rate. Electronic time stamps were plotted with specific signatures, including time of medication administration, procedure beginning and completion, physician interventions, and adverse events.

Before study blinding was broken, 3 investigators evaluated each graph to code the presence or absence of hypoxia and respiratory depression. Hypoxia was defined a priori as an SpO2 level of less than 93% for 15 seconds or greater. Respiratory depression was defined a priori as an ETCO2 level of 50 mm Hg or greater, an absolute increase or decrease from baseline of 10% or greater, or a loss of waveform for 15 seconds or greater. We disqualified graphs if they had greater than 35% data loss, unless all 3 evaluators agreed that there was unequivocal evidence of hypoxia or respiratory depression. Lost data were typically due to patient movement (ie, dislodgement of the cannula) or blood pressure cuff insufflation.

### Primary Data Analysis

We analyzed our data descriptively and using $\chi^2$, with $P<.05$ considered significant. All analyses were with SPSS version 10 (SPSS, Chicago, IL).

Previous research has reported rates of hypoxia during ED propofol sedation ranging from 15% to 30%.14-17 To identify a 15% decrease in hypoxia from a 20% presumed baseline, we calculated that we would need 72 patients in each arm (assuming a 1-tailed analysis, a power of 80%, and an $\alpha$ of 5%).

### RESULTS

#### Characteristics of Study Subjects

Two hundred ten patients were screened during the study period, of whom 132 composed the study group (Figure 2).
Patient characteristics were similar between the 2 groups (Table 1). Hypoxia occurred in 44 subjects overall (33%; 95% confidence interval [CI] 25% to 41%).

Main Results
Although respiratory depression occurred at similar rates between groups, hypoxia was significantly more frequent in the blinded capnography group (Table 2). Seventeen patients in the nonblinded group and 27 patients in the blinded group experienced a SpO2 level of less than or equal to 93% (effect size 17%; P= .035; 95% CI 1.3% to 33%).

Regardless of study group, all patients who developed hypoxia first exhibited respiratory depression (Table 2). Accordingly, respiratory depression was 100% sensitive in predicting hypoxia (95% CI 90% to 100%). There were 32 subjects with “false-positive” results, who exhibited respiratory depression but did not ultimately develop hypoxia, and thus capnography was 64% specific (95% CI 53% to 73%).

For patients with hypoxia, the median time between the onset of respiratory depression and the onset of hypoxia was 60 seconds (range 5 to 240 seconds).

The majority of patients who developed respiratory depression had an ETCO2 change greater than 10% from baseline (Table 3). In this study, a loss of waveform was most likely to lead to hypoxia.

Table 1. Patient characteristics.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Capnography (n=68)</th>
<th>Blinded Capnography (n=64)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median age, y</td>
<td>31 (Range 18–72)</td>
<td>37 (Range 18–88)</td>
</tr>
<tr>
<td>Sex (females, No.)</td>
<td>35</td>
<td>27</td>
</tr>
<tr>
<td>Median weight, kg</td>
<td>81 (Range 52–157)</td>
<td>75 (Range 40–220)</td>
</tr>
<tr>
<td>Abscess incision and drainage (%)</td>
<td>32 (47)</td>
<td>27 (43)</td>
</tr>
<tr>
<td>Fracture reduction (%)</td>
<td>8 (12)</td>
<td>11 (17)</td>
</tr>
<tr>
<td>Joint reduction (%)</td>
<td>28 (41)</td>
<td>26 (40)</td>
</tr>
<tr>
<td>Mean initial propofol dose, mg/kg</td>
<td>0.86 (SD=0.2)</td>
<td>0.92 (SD=0.18)</td>
</tr>
<tr>
<td>Mean total propofol dose, mg/kg</td>
<td>1.4 (SD=0.43)</td>
<td>1.5 (SD=0.56)</td>
</tr>
<tr>
<td>Median Ramsey scores (90 s after the last dose of preprocedure medication)</td>
<td>4 (Range 1–6)</td>
<td>4 (Range 1–6)</td>
</tr>
<tr>
<td>Median time from first dose of medication to return to baseline alertness, min</td>
<td>13 (Range 3–29)</td>
<td>14 (Range 4–32)</td>
</tr>
</tbody>
</table>

Table 2. Respiratory depression and hypoxia.

<table>
<thead>
<tr>
<th></th>
<th>Capnography (%) (n=68)</th>
<th>Blinded Capnography (%) (n=64)</th>
<th>Difference (%) (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Respiratory depression</td>
<td>39 (57)</td>
<td>37 (58)</td>
<td>1 (–16 to 17)</td>
</tr>
<tr>
<td>Hypoxia</td>
<td>17 (25)</td>
<td>27 (42)</td>
<td>17 (1.3 to 33)</td>
</tr>
<tr>
<td>No hypoxia</td>
<td>22 (32)</td>
<td>10 (16)</td>
<td>16 (2 to 38)</td>
</tr>
<tr>
<td>No respiratory depression</td>
<td>29 (43)</td>
<td>27 (42)</td>
<td>1 (–16 to 17)</td>
</tr>
<tr>
<td>Hypoxia</td>
<td>0</td>
<td>0</td>
<td>0 (–6 to 5)</td>
</tr>
<tr>
<td>No hypoxia</td>
<td>29 (43)</td>
<td>27 (42)</td>
<td>1 (–16 to 17)</td>
</tr>
</tbody>
</table>
Our observed rate of hypoxia (32.5%) was higher than that observed in most other studies of propofol for ED procedural sedation. A rate of hypoxia more consistent with previous studies of propofol for ED procedural sedation was not underpowered. However, we found a significant difference in our main outcome, leaving the study not unduly large.

Our observed rate of hypoxia (32.5%) was higher than that observed in most other studies of propofol for ED procedural sedation. A rate of hypoxia more consistent with previous studies may have produced a smaller, nonsignificant difference between groups.

We doubt that coadministered opioids are responsible for our high rate of hypoxia because no patient received morphine or fentanyl with 30 minutes of propofol and our doses were not unduly large.

It is also possible that our continuous electronic data collection using the Capnostream 20 influenced the rate of hypoxia because it would detect episodes that might otherwise be missed through recording only at spaced intervals or through human inattention or error.

We believe it unlikely that any device error contributed to our higher-than-expected rates of hypoxia and respiratory depression because we used strict definitions for respiratory depression and hypoxia and a three-physician team to code each graph. This method helped minimize the number of spurious readings that were measured.

It is possible that, if our clinicians had used greater amounts of supplemental oxygen, there would have been less overall hypoxia. However, the current literature is inconclusive about the effect of preoxygenation or high-flow oxygen delivery on sedation-associated hypoxia. Future research should address this issue.

We chose a priori an SpO2 of 93% as our baseline level for hypoxia because we believe that most physicians will pay close attention and potentially intervene at this level. A lower threshold would have resulted in less overall hypoxia.

Our physicians are trained to consider a 10% change from ETCO2 baseline as respiratory depression. Previous studies have used a 10-mm Hg ETCO2 change from baseline as criteria for respiratory depression. Post hoc analysis from our previous propofol study showed an increase in sensitivity in the prediction of a hypoxic event when this criterion was applied. It is possible that the use of a less stringent set of ETCO2 criteria would have decreased the rate of physician intervention for respiratory depression (in the nonblinded group). Fewer physician interventions may have decreased the recorded difference in the rate of hypoxia between the two groups.

We excluded patient graphs that were missing more than 35% of the data unless there was unequivocal evidence of respiratory depression or hypoxia. We regard this as a reasonable threshold; however, alternative criteria for excluding patients with missing data may have affected our results in either direction.

**DISCUSSION**

Physicians performing ED procedural sedation with propofol decreased the rate of hypoxic events by using capnography in conjunction with standard monitoring. The measured difference (17%) is both statistically and clinically significant. Capnographic respiratory depression occurred before the onset of hypoxia and was temporally linked to subsequent hypoxic events.

We found that capnography was 100% sensitive for predicting hypoxia because every patient with hypoxia first exhibited capnographic evidence of respiratory depression. However, capnography exhibited imperfect specificity (64%) because not all patients with respiratory depression ultimately developed hypoxia. Further research should address which specific capnographic changes are the most predictive of hypoxia.

Two early small studies of capnography during ED sedation by Wright and later by Hart et al suggested its ability to identify ventilatory dysfunction.
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studies between 2001 and 2003, using capnography to detect the presence of respiratory depression. In these studies, 41% to 48% of the patients experienced changes in ETCO₂ consistent with respiratory depression; however, the majority of these patients did not develop hypoxia.

Recent studies have suggested that capnographic changes consistent with respiratory depression occur before the onset of hypoxia. Anderson et al. administered propofol to 125 ED pediatric patients and found that continuous capnography detected 10 of 14 airway and respiratory adverse events before pulse oximetry or clinical observation. A study by Burton et al. was halted after 60 patients because an interim analysis found that 17 of 19 patients who became hypoxic demonstrated capnographic changes indicative of hypoventilation or apnea at or before the hypoxic event. Lightdale et al. evaluated the utility of capnography in children undergoing procedural sedation and analgesia in the endoscopy suite. Patients were divided into 2 groups. In the treatment group, an independent observer signaled the endoscopy team if the patient had an abnormal capnographic reading. In the control group, the treatment team was not given any capnographic information. The authors observed a significantly lower rate of hypoxic events in the treatment group compared with the control group.

We conducted 2 previous studies that used capnography in ED procedural sedation and analgesia. Both studies demonstrated that capnography accurately predicts the onset of a hypoxic event and that emergency physicians (blinded to capnography) do not recognize respiratory depression in patients until hypoxia develops. This is potentially concerning, given the risk of respiratory depression associated with the opioids and sedative/hypnotics used in procedural sedation and analgesia.

In this study, many patients (63%) who had capnography-documented respiratory depression had a decrease in ETCO₂ greater than 10%. These patients all received propofol, a sedative-hypnotic that is associated with hypopneic respiratory depression. In this type of respiratory depression, tidal volume is depressed proportionally greater than respiratory rate, resulting in an increase in the dead space/tidal volume ratio, decreasing ETCO₂ in the face of increasing arterial hypercarbia. This effect has been seen in previous studies using sedative-hypnotics and capnography. We recommend that physicians pay particular attention to decreases in ETCO₂ with administration of sedative-hypnotics during procedural sedation and analgesia because this may herald hypoxia.

In this study, every patient who developed hypoxia had a corresponding ETCO₂ change. In our previous studies, a minority of patients had hypoxia without capnographic changes. We believe that the increased sensitivity of the near-continuous electronic data capture with the Capnostream 20 allowed us to measure this effect.

The median time between the onset of respiratory depression and an incidence of hypoxia was 60 seconds (range 5 to 240 seconds). This study was not designed to measure the mean gap between respiratory depression and hypoxia. However, it is an important observation; for many patients, the physicians had an ample amount of time to identify capnographic evidence of respiratory depression and intervene. Conversely, it is possible that some incidences of hypoxia occurred so quickly after a corresponding capnographic change that the physicians could not respond rapidly enough to prevent them. This study was not designed to evaluate this effect.

Capnography can provide early warning of ventilatory abnormalities, alerting physicians to respiratory depression before the onset of a hypoxic event. Using capnography in this study, emergency physicians improved patient safety by decreasing the rate of hypoxic events associated with procedural sedation and analgesia.

In our study, a number of patients had respiratory depression and hypoxia and the treating physician did not intervene, with the episodes resolving spontaneously. If every incidence of respiratory depression had led to an intervention, it is possible that there would have been less hypoxia. Further investigation is needed to distinguish those ventilatory abnormalities that lead to hypoxia versus those that do not, as well as to determine the characteristics of hypoxic events that persist versus those that spontaneously resolve.

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Author contributions: KD, JM, and CRC conceived the study and designed the trial. KD, CRC, and PD supervised the conduct of the trial and data collection. KD, CRC, and PD managed the data, including quality control. PD and DL provided statistical advice on study design and analyzed the data. KD drafted the article. CRC and JM provided editorial support and contributed substantially to its revisions. KD takes responsibility for the paper as a whole.

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