

# The Utility of Supplemental Oxygen During Emergency Department Procedural Sedation With Propofol: A Randomized, Controlled Trial

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**Study objective:** We determine whether supplemental oxygen reduces the incidence of hypoxia by 20% compared with breathing room air in adult study patients receiving propofol for emergency department procedural sedation.

**Methods:** Patients were randomized to receive either supplemental oxygen or compressed air by nasal cannula at 3 L per minute. Physicians were blinded to the gas used and end tidal CO<sub>2</sub> (ETCO<sub>2</sub>) data. Respiratory depression was defined a priori as oxygen saturation less than or equal to 93%, an ETCO<sub>2</sub> level of greater than or equal to 50 mm Hg, an absolute ETCO<sub>2</sub> change from baseline of greater than or equal to 10 mm Hg, or loss of the ETCO<sub>2</sub> waveform.

**Results:** Of the 110 patients analyzed, 56 received supplemental oxygen and 54 received room air. Ten (18%) patients in the supplemental oxygen group and 15 (28%) patients in the compressed air group experienced hypoxia ( $P=.3$ , effect size=10%, 95% confidence interval -24% to 7%). Twenty-seven patients (20 supplemental oxygen; 7 room air) met ETCO<sub>2</sub> criteria for respiratory depression but did not become hypoxic. Physicians identified respiratory depression in 23 of 25 patients who developed hypoxia compared with only 1 of 27 patients who met ETCO<sub>2</sub> criteria for respiratory depression but who did not have hypoxia. One patient in the supplemental oxygen group experienced a transient arrhythmia and had a short apneic episode, both of which resolved spontaneously. The patient was admitted for observation.

**Conclusion:** Supplemental oxygen (3 L/minute) trended toward reducing hypoxia in adult study patients; however, the 10% difference observed was not statistically significant and was below our a priori 20% threshold. Blinded capnography frequently identified respiratory depression undetected by the treating physicians. [Ann Emerg Med. 2008;52:1-8.]

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## INTRODUCTION

### Background

Throughout the past decade, the need to provide safe and effective procedural sedation has prompted an increasing number of emergency department (ED) clinical trials and the introduction of new agents, techniques, and monitoring devices. Yet, despite the knowledge gained by scientific study and clinical experience, early detection of respiratory depression and prevention of hypoxia remains a challenge.<sup>1</sup> To reduce the incidence of hypoxia, the American Society of Anesthesiology recommends the use of supplemental oxygen for patients

undergoing deep sedation and suggests it be considered during moderate sedation.<sup>2</sup> Although these recommendations seem intuitive, there is a paucity of information about the risks and benefits of supplemental oxygen during ED procedural sedation.

The goal of supplemental oxygen is to increase oxygen reserves, thereby delaying or preventing the onset of hypoxia. However, increasing oxygen reserves is not without risk. It has been shown that superoxygenated patients desaturate only after prolonged apnea.<sup>3,4</sup> This negates the use of pulse oximetry as an early warning device for respiratory depression,<sup>2,5,6</sup> which is concerning in light of the fact that emergency physicians rarely recognize respiratory depression in sedated patients who do not become hypoxic.<sup>7</sup>

**Editor's Capsule Summary***What is already known on this topic*

Though supplemental oxygen does not reduce the rate of complicating hypoxia during sedation with midazolam and fentanyl, it might do so for propofol, which is typically used to induce a deeper level of sedation.

*What question this study addressed*

Does 3L/min of oxygen by nasal cannula affect the frequency of oxygen desaturation during propofol sedation?

*What this study adds to our knowledge*

Desaturation occurred less frequently in the oxygen group (18%) than control group (28%), though this difference was smaller than the 20% difference deemed important by the investigators.

*How this might change clinical practice*

Although not definitive, this best available study suggests that adding 3 L per minute of supplemental oxygen during propofol sedation produces only a minor decrease in the risk of hypoxia, if any.

*Research we'd like to see*

Replication of this study using 100% preoxygenation.

In the only other prospective study specifically designed to evaluate the use of supplemental oxygen during ED procedural sedation and analgesia, we found that 2 L of supplemental oxygen did not reduce the incidence of hypoxia by 20% in adult patients receiving midazolam and fentanyl.<sup>7</sup> It is not clear whether these results can be extrapolated to other agents, particularly propofol, which has a higher incidence of respiratory depression.<sup>8</sup>

**Importance**

If supplemental oxygen can limit the incidence or severity of hypoxia during procedural sedation with propofol, without hindering early recognition of respiratory depression, it should be incorporated into standard ED procedural sedation protocols. If supplemental oxygen prevents hypoxia but interferes with the physician's ability to detect respiratory depression, then additional precautions such as monitoring end tidal carbon dioxide (ETCO<sub>2</sub>) may be indicated. If supplemental oxygen does not reduce the incidence of hypoxia, its use should be abandoned.

**Goals of This Investigation.** The goal of this study was to determine whether supplemental oxygen delivered at 3 L per minute by nasal cannula would reduce the incidence of hypoxia by 20% in adult patients receiving propofol for procedural sedation. We also evaluated whether physicians blinded to capnographic data are able to recognize respiratory depression during procedural sedation. Finally, in a preplanned secondary

analysis, we compared the relative accuracy of capnography in predicting hypoxia when the criterion of a 10-mm Hg absolute change in ETCO<sub>2</sub> from baseline is narrowed to a 10% absolute change in ETCO<sub>2</sub> from baseline.

**MATERIALS AND METHODS****Study Design**

This was a prospective, randomized, double-blind, placebo-controlled study conducted between November 2005 and October 2006. The institutional review board approved the study.

**Setting and Selection of Participants**

The study was performed in the ED at the Albert Einstein Medical Center, a Level I trauma center located in Philadelphia, PA. The ED features a well-established emergency medicine residency program and has an annual census of approximately 75,000 patient visits.

All patients older than 18 years and receiving propofol to facilitate a painful procedure were eligible for the study. Enrollment occurred after the attending physician made the decision that propofol would be safe and appropriate for procedural sedation. Consecutive patients who met inclusion criteria were enrolled 24 hours a day, 7 days a week during the study period.

Patients were excluded if they had severe chronic obstructive pulmonary disease, long-term oxygen use, hemodynamic instability, respiratory distress, pregnancy, allergy to any of the study drugs, or inability to provide informed consent.

Written informed consent was obtained from each subject.

Patients were randomized to receive either supplemental oxygen or room air at 3 L per minute by nasal cannula. Randomization was done with a computerized randomization table. Patients were assigned to their respective groups sequentially down a numbered list.

Procedural sedation was performed according to standard ED protocol. For this study, a research associate was present for the entire patient encounter and was responsible for ensuring appropriate patient selection, randomization, and data collection. The research associates are non-board certified physicians who received specific training about procedural sedation, the study protocol, and data collection techniques, including identifying interventions by the treatment team to improve oxygenation or ventilation.

After collection of baseline data, patients were randomized to receive room air or oxygen by nasal cannula at 3 L per minute. To ensure that the treatment team was blinded to the type of gas being administered, the gases were delivered from one of 2 identical D-tanks marked "A" and "B." The initial dose of intravenous propofol was 1 to 1.5 mg/kg (ideal body weight). We chose this range according to our previous study, during which we found that 1.0 mg/kg of propofol often produced inadequate sedation. Subsequent doses of 0.5 mg/kg were administered until the desired level of sedation was achieved. Once the patient was adequately sedated, the procedure was

performed. Patients were closely monitored until back to baseline alertness.

### Data Collection

Age, sex, medical history, medications, and allergies; type of procedure performed; and sedation and procedure times were recorded by the research associates with a standardized data collection instrument. Procedure time was defined as the time from initial propofol administration until the patient returned to baseline alertness. The research associates measured alertness levels with a 6-point Ramsay scale, with 1 indicating agitation and 6 indicating unresponsiveness. This scale has been validated in ICU patients and used in a number of studies of ED procedural sedation and analgesia.<sup>7,9-11</sup> A Ramsay score was recorded at baseline, 90 seconds after completion of drug administration, and when it appeared the patient was back to baseline alertness.

Vital signs (pulse rate, respiratory rate, and blood pressure), oxygen saturation, and  $\text{ETCO}_2$  levels were recorded at baseline and every 5 minutes until the patient returned to baseline alertness.  $\text{ETCO}_2$  was monitored with the NPB-Microstream 75  $\text{ETCO}_2$  monitor (Nellcor Puritan Bennett Inc., Pleasanton, CA) connected to a nasal cannula capable of delivering compressed gases and fitted with an oral  $\text{ETCO}_2$  sampler to accommodate mouth breathers (Smart Capnoline O<sub>2</sub> Nasal Cannulas; Oridion Inc, Brussels, Belgium). The NPB-Microstream 75  $\text{ETCO}_2$  monitor samples continuously at 50 mL per minute and can process up to 150 breaths/min. In an effort to determine how well procedural sedation providers recognize respiratory depression with standard monitoring techniques (ie, observation, vital signs, pulse oximetry), the treatment team was kept blinded to  $\text{ETCO}_2$  levels.

### Outcome Measures

Respiratory depression was defined a priori as oxygen saturation less than 93%, an  $\text{ETCO}_2$  level of greater than 50 mm Hg, an absolute  $\text{ETCO}_2$  change from baseline of greater than 10 mm Hg, or loss of the  $\text{ETCO}_2$  waveform. These criteria were considered present if they occurred any time during the procedure, regardless of their duration. When any of these criteria occurred, the patient's vital signs, oxygen saturation, and  $\text{ETCO}_2$  level were recorded. The research associates also recorded these characteristics if any member of the treatment team verbalized that the patient was experiencing respiratory depression or provided an intervention to assist breathing, including verbal or physical stimulation, airway realignment, use of additional oxygen (from a wall source) or airway adjuncts, assisted ventilation, or intubation. Other adverse events, including hypotension, bradycardia, vomiting, prolonged ED stay (>2 hours after the procedure), or admissions, were also recorded on the data collection instruments.

The treatment team was unaware that the research associates were evaluating their (ie, the treatment team's) ability to recognize respiratory depression with standard PSA monitoring. ED personnel did not provide consent for the study because knowledge of this aspect of the protocol could result in

significant bias. The institutional review board agreed that because individual staff members would not be identified in any way, staff consent was not necessary.

### Primary Data Analysis

Data analysis was performed with SPSS statistical software (SPSS, Inc., Chicago, IL). The incidence of hypoxia in each group was compared with the 2-sample test of proportions. The number of interventions to treat respiratory depression in each group was compared with the  $\chi^2$  test. Data are presented using 95% confidence intervals where appropriate.  $P < .05$  was used to denote statistical significance. The study was powered to test the null hypothesis that there is no difference in the incidence of hypoxia in patients receiving supplemental oxygen and those receiving room air during ED PSA using propofol. Previous PSA studies evaluating propofol have found that hypoxia occurs in 8% to 30% of patients.<sup>12-17</sup> For our power calculation, we assumed that lowering the absolute incidence of hypoxic events by 20% would be clinically significant. Using Fisher's exact test of 2 means (1-tailed test), with group 1 at 25% and group 2 at 5%, a power of 80%, and an  $\alpha$  of 0.05, we calculated that the study would require approximately 48 patients per group.

## RESULTS

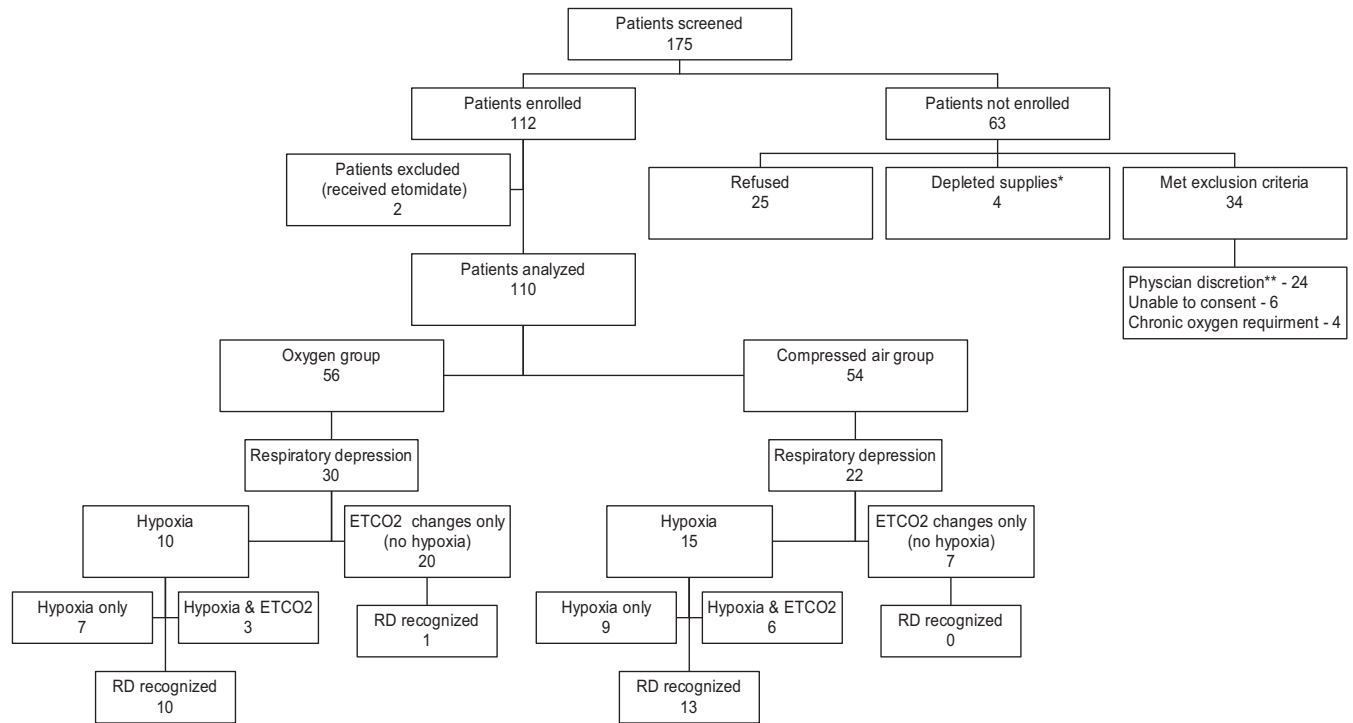
### Characteristics of Study Subjects

Research associates screened 175 patients during the 12-month study period. Of these, 112 were enrolled in the study. Two patients were subsequently excluded because they received a nonstudy medication (etomidate) for sedation, leaving 110 patients for analysis (Figure). The 2 groups were similar with respect to age, sex, and weight. Abscess incision and drainage and fracture and joint reduction accounted for all procedures. There were no significant differences between the groups in the type or duration of procedures performed, the mean initial and total dose of propofol administered, the depth of sedation achieved, or the time to return to baseline alertness (Table 1).

Ten patients in the supplemental oxygen group and 15 patients in the room air group experienced oxygen saturations less than 93% ( $P = .3$ ; effect size = 10%; 95% CI -24% to 7%).

Of the patients who met 1 or more criteria for respiratory depression, there were no differences between those patients receiving supplemental oxygen and those receiving room air (Table 2). Twenty-seven of 110 (24.5%) study patients met 1 or more  $\text{ETCO}_2$  criteria for respiratory depression but did not experience hypoxia (Table 2). Of the 25 patients whose oxygen saturation decreased below 93%, 9 had  $\text{ETCO}_2$  changes consistent with respiratory depression before the onset of hypoxia. Tables 3-5 provide a detailed summary of all  $\text{ETCO}_2$  data.

Overall, physicians identified 24 of the 52 total patients who experienced 1 or more criteria of respiratory depression. In the subset of patients who became hypoxic, physicians identified 23 of 25 patients, including all 10 patients in the supplemental oxygen group and 13 of 15 patients in the room air group (Table 6). In contrast, physicians detected respiratory depression



**Figure.** Schematic representation of study results.

\*Depleted supplies: Ran out of nasal cannula

†Physician discretion: Physician felt that the patient was not a candidate for procedural sedation or propofol

RD, Respiratory depression.

**Table 1.** Patient characteristics.

Characteristic	Supplemental Oxygen (n=56)	Room Air (n=54)
Median age, y (range)	37 (19-86)	37 (18-75)
Sex, female, No.	33	29
Median weight, kg (range)	86 (49-145)	79 (43-134)
Abscess incision and drainage (%)	37 (66)	32 (59)
Fracture reduction (%)	6 (10)	9 (17)
Joint reduction (%)	13 (23)	7 (13)
Mean initial propofol dose (mg/kg)	1.19 (SD=0.32)	1.33 (SD=0.32)
Mean total propofol dose (mg/kg)	1.71 (SD=0.66)	1.99 (SD=0.79)
Median Ramsey scores 90 s after the last dose of preprocedure medication (range)	5 (2-6)	5 (2-6)
Median time from first dose of medication to return to baseline alertness, min (range)	10 (3-28)	12 (4-35)

in only 1 of 27 patients who met 1 or more of the ETCO<sub>2</sub> criteria for respiratory depression but who did not become hypoxic.

An absolute ETCO<sub>2</sub> change of greater than 10 mm Hg identified 9 of 25 patients who experienced hypoxia (36% sensitive [95% CI 18% to 57%] and 68% specific [95% CI

**Table 2.** Respiratory depression.

Patients	Supplemental Oxygen (n=56)	Room Air, % (n=54)	Effect Size, % (95% CI)
Total number of patients meeting 1 or more criteria* for respiratory depression (%)	30 (53)	22 (40)	8 (-5 to 31)
Patients meeting both oxygen saturation and ETCO <sub>2</sub> criteria* for respiratory depression (%)	3 (5)	6 (11)	3 (-16 to 45)
Patients meeting only oxygen saturation criteria* for respiratory depression (%)	7 (12)	9 (16)	2 (-17 to 9)
Patients meeting only ETCO <sub>2</sub> criteria* for respiratory depression (%)	20 (36)	7 (12)	14 (-7 to 38)

\*Respiratory depression: PO<sub>2</sub> <93%, ETCO<sub>2</sub> >50 mm Hg, an absolute ETCO<sub>2</sub> change from baseline of >10 mm Hg, or loss of the ETCO<sub>2</sub> waveform.

57% to 77%]; positive predictive value [PPV]=32%, negative predictive value [NPV]=67%). An absolute ETCO<sub>2</sub> change from baseline of greater than 10% would have identified 18 of the 25 patients before they developed hypoxia (sensitivity 72% [95% CI 59% to 93%], specificity 47% [95% CI 36% to 58%]; PPV=37%, NPV=80%).

**Table 3.** ETCO<sub>2</sub> changes.

ETCO <sub>2</sub> Changes	Supplemental Oxygen (n=56)*	Room Air (n=54)*
ETCO <sub>2</sub> >50 mm Hg (number of patients who became hypoxic)	1 (0)	2 (1)
ETCO <sub>2</sub> >10 mm Hg above baseline (number of patients who became hypoxic)	4 (0)	2 (2)
ETCO <sub>2</sub> >10 mm Hg below baseline (number of patients who became hypoxic)	19 (3)	11 (4)
Loss of the ETCO <sub>2</sub> Waveform (number of patients who became hypoxic)	1 (0)	1 (0)

\*Some patients met more than 1 criterion.

One patient in the supplemental oxygen group received a brief period of assisted ventilation. The treating physician thought the patient became apneic, but there was no loss of the ETCO<sub>2</sub> waveform indicative of apnea. The patient received a single 1.05 mg/kg dose of propofol for incision and drainage of a buttock abscess; she was not given any other medications. Three minutes after she received propofol, her oxygen saturation dropped to 85%, which was followed 6 minutes later by a 14-mm Hg increase in ETCO<sub>2</sub>. She also experienced a transient (<10 seconds) sinus pause that resolved spontaneously and postprocedure wheezing that resolved with 2 albuterol treatments and intravenous steroids. She was admitted for observation and discharged the next day without further sequelae. Six patients (3 in each group) developed mild, transient hypotension (lowest systolic blood pressure 84 mm Hg). No patient in either group experienced bradycardia or vomiting, and no patients were intubated. There were no other adverse events.

## LIMITATIONS

We administered 3 L per minute of oxygen to the subjects in the treatment group. Providing a higher concentration of supplemental oxygen may have resulted in a lower incidence of hypoxia.

The mean initial and total propofol doses were slightly higher in the room air group (Table 1), which may have contributed to the difference in the incidence of hypoxia observed between the 2 groups.

We defined hypoxia as an oxygen saturation of less than 93%. Although this level is higher than the traditional definition of hypoxia (ie, 90%), we believe that an oxygen saturation of 93% would prompt most clinicians to provide some intervention to improve oxygenation and or ventilation. Using a lower oxygen saturation level may have increased the incidence of hypoxia.

Our study was powered to detect a 20% reduction in the incidence of hypoxia in patients receiving supplemental oxygen compared with patients breathing room air. Had we chosen a

smaller difference and enrolled more patients, we might have found a statistical difference.

Members of the clinical staff were blinded to the type of gas being administered and to the ETCO<sub>2</sub> monitor, and they were unaware that their ability to recognize respiratory depression was being evaluated. Nevertheless, it is possible that knowing the study was evaluating the use of supplemental oxygen heightened their awareness for identifying respiratory depression. However, the potential for heightened awareness would be the same whether the patient was receiving supplemental oxygen or room air and therefore would not be expected to affect the results.

The research associates were not blinded to the purpose of this study, which could have resulted in bias during data collection. However, the research associates made no patient care decisions; they were present only to ensure protocol adherence and accurate data collection. In addition, all research associates participating in this study were physicians who received training specifically directed at identifying a physician intervention for respiratory depression.

## DISCUSSION

Supplemental oxygen (3 L/minute) trended toward reducing hypoxia in adult study patients; however, the 10% difference observed was not statistically significant and was below our a priori 20% threshold. To our knowledge, this is the first study specifically designed to evaluate the use of supplemental oxygen during procedural sedation that has shown a potential benefit to its use. We performed a previous study of procedural sedation and analgesia with midazolam and fentanyl, in which the use of supplemental oxygen did not lower incidence of hypoxia.<sup>7</sup>

In our previous study, we found that 2 L of supplemental oxygen by nasal cannula failed to reduce the incidence of hypoxia in patients receiving midazolam and fentanyl for procedural sedation and analgesia (13% in the supplemental oxygen group versus 14% in the room air group; *P*=nonsignificant).<sup>7</sup> This study was powered to detect a 20% difference in the incidence of hypoxia, but only 13.9% of all patients in the study became hypoxic. A lower than expected incidence of hypoxia weakened the study by making it impossible to demonstrate our a priori definition of clinical significance.

There are few other studies that support or discourage the use of supplemental oxygen during ED procedural. Three previous studies have compared patients with and without supplemental oxygen and found conflicting results about the impact on respiratory depression and hypoxia. However, these studies were neither blinded nor randomized and were not designed to specifically evaluate the value of supplemental oxygen.<sup>8,12,18</sup>

The current study was powered to detect a 20% difference in the incidence of hypoxia between the 2 groups. We chose this difference according to our belief that most emergency physicians would consider a 20% reduction in the incidence of hypoxia to be clinically significant and because it allowed us to design a study that

**Table 4.** Patients with an absolute  $\text{ETCO}_2$  change from baseline of greater than 10 mm Hg without hypoxia.

Supplemental Oxygen			Room Air		
Patient No.	Baseline $\text{ETCO}_2$ (mm Hg)	Highest or Lowest $\text{ETCO}_2$ Value (mm Hg)	Patient No.	Baseline $\text{ETCO}_2$ (mm Hg)	Highest or Lowest $\text{ETCO}_2$ Value (mm Hg)
1	36	23	19	37	7
2	44	30	20	37	27
3	35	17	21	37	22
8	18	47	84	37	20
16	41	28	85	35	20
35	35	5	98	38	17
38	34	47	101	38	28
42	40	8			
62	38	12			
63	34	8			
66	33	44			
67	47	8			
74	38	6			
75	41	10			
76	42	8			
83	41	28			
88	42	52			
97	41	3			
105	39	25			
107	32	21			

**Table 5.** Patients with an absolute  $\text{ETCO}_2$  change from baseline of greater than 10 mm Hg with hypoxia.

Supplemental Oxygen			Room Air		
Patient No.	Baseline $\text{ETCO}_2$ (mm Hg)	Highest or Lowest $\text{ETCO}_2$ Value (mm Hg)	Patient No.	Baseline $\text{ETCO}_2$ (mm Hg)	Highest or Lowest $\text{ETCO}_2$ Value (mm Hg)
47	37	11	25	38	12
48	37	10	36	39	53
90	39	2	55	37	47
			58	37	16
			60	42	12
			65	38	14

required a reasonable number of subjects. As it turns out, we found that supplemental oxygen decreases the incidence of hypoxia by 10%. Thus, according to our definition of clinical significance (20%) and subsequent power calculation, the study failed to show a statistically significant difference in the incidence of hypoxia in patients receiving supplemental oxygen compared with those breathing room air. Nevertheless, there appears to be a trend toward a lower rate of hypoxia (10%) when supplemental oxygen is given. This trend may be enough to prompt some clinicians to administer supplemental oxygen when using propofol for procedural sedation. A larger study will be needed to confirm whether a difference of 10% truly exists.

Physicians identified the presence of respiratory depression in 23 of 25 patients who experienced hypoxia. In the 2 patients whose hypoxic events went unrecognized, the duration of hypoxia was brief (<60 seconds) and the severity was mild (lowest oxygen saturation was 88%). In our previous study using midazolam and fentanyl, physicians failed to identify hypoxia in 3 of 11 patients whose oxygen saturation decreased

below 92%.<sup>7</sup> The missed hypoxic episodes in that study were also short lived (<60 seconds) and mild (lowest oxygen saturation was 87%). At that time, we surmised that the ED staff simply missed these brief episodes of hypoxia or that the physicians managing the cases decided to initially observe rather than treat mild, transient hypoxia. Our study design does not allow us to answer this question for either study but does suggest that giving a patient continuous pulse oximetry does not guarantee that the ED staff will identify all episodes of hypoxia.

In patients with unobstructed airways, hypoventilation causes  $\text{ETCO}_2$  levels to increase,<sup>12</sup> whereas hypoventilation in the presence of a developing airway obstruction produces a decrease in  $\text{ETCO}_2$  or loss of the  $\text{ETCO}_2$  waveform.<sup>8</sup> It has been suggested that an  $\text{ETCO}_2$  level of greater than 50 mm Hg, an absolute  $\text{ETCO}_2$  change from baseline of greater than 10 mm Hg, or loss of the  $\text{ETCO}_2$  waveform may identify patients at risk for developing clinically significant respiratory depression,<sup>19</sup> signaling clinicians to intervene by stimulating breathing (for increasing  $\text{ETCO}_2$ ), repositioning the airway (for decreasing

**Table 6.** Physician recognition\* of patients experiencing respiratory depression.<sup>†</sup>

Patients	Supplemental	
	Oxygen (n=56)	Room Air (n=54)
Number of patients identified with respiratory depression/total number of patients who met 1 or more criteria for respiratory depression	11/30	13/22
Number of patients identified with respiratory depression/total number of patients who met only oxygen saturation criteria for respiratory depression	7/7	7/9
Number of patients identified with respiratory depression/total number of patients who met both oxygen saturation and ETCO <sub>2</sub> criteria for respiratory depression	3/3	6/6
Number of patients identified with respiratory depression/total number of patients who met only ETCO <sub>2</sub> criteria for respiratory depression	1/20	0/7

\*The treatment team was given credit for identifying respiratory depression if any member of the team verbalized that the patient was experiencing respiratory depression or provided an intervention to assist breathing, including verbal or physical stimulation, airway realignment, use of additional oxygen or airway adjuncts, assisted ventilation, or intubation.

<sup>†</sup>Criteria for respiratory depression: Oxygen saturation of <93%, ETCO<sub>2</sub> level of >50 mm Hg, an absolute ETCO<sub>2</sub> change from baseline of >10 mm Hg, or loss of the ETCO<sub>2</sub> waveform.

ETCO<sub>2</sub> or loss of the ETCO<sub>2</sub> waveform), or withholding additional sedatives.<sup>20</sup> The ability of ETCO<sub>2</sub> to identify respiratory depression before the onset of hypoxia is supported by a number of recent studies of ED procedural sedation.

In a study of children undergoing ED procedural sedation with propofol for orthopedic reduction, Anderson et al<sup>21</sup> found that capnography detected apnea in 5 of 5 patients and airway obstruction in 6 of 10 patients *before* clinical examination or pulse oximetry. In 2006, Burton et al<sup>22</sup> evaluated the ability of ETCO<sub>2</sub> monitoring to detect adverse respiratory events before standard sedation monitoring practices. In this study, ETCO<sub>2</sub> changes consistent with respiratory depression occurred in 17 of 20 patients (85%) who experienced an adverse respiratory event. The ETCO<sub>2</sub> changes occurred 12 to 217 seconds before the onset of hypoxia or apnea in 14 of these patients and with the onset of hypoxia in 3 patients. In our study, we found that 9 of the 25 patients (41%) who developed hypoxia had preceding ETCO<sub>2</sub> changes meeting our definition of respiratory depression (Table 6). Unfortunately, the capnography monitor used in our study does not allow us to provide exact intervals between ETCO<sub>2</sub> changes and the onset of hypoxia.

In an attempt to improve the sensitivity of ETCO<sub>2</sub> monitoring for identifying which patients may become hypoxic, we performed a secondary analysis comparing the sensitivity and specificity of an absolute change in ETCO<sub>2</sub> from baseline of greater than 10 mm Hg to an absolute change from baseline of greater than 10% as a criterion for respiratory depression. We

found that using an absolute ETCO<sub>2</sub> change from baseline of greater than 10% identified twice the number of patients who became hypoxic. We suggest identifying an ETCO<sub>2</sub> “safe zone” by calculating the ETCO<sub>2</sub> level 10% above and 10% below a patient’s baseline. As long as the patient’s ETCO<sub>2</sub> remains in this safe zone, no intervention would be needed. An ETCO<sub>2</sub> level above or below this range would prompt the clinician to reposition the airway, stimulate the patient, and consider the need for other interventions as needed.

Our study was not designed to evaluate the use of an ETCO<sub>2</sub> safe zone, but our data seem compelling, and we plan to test this concept in a controlled trial. Using an absolute change in ETCO<sub>2</sub> from baseline of greater than 10% results in a lower specificity. However, we believe that a greater sensitivity for identifying which patients will experience hypoxia outweighs the loss of specificity.

In the current study, 27 patients experienced ETCO<sub>2</sub> changes consistent with respiratory depression but never became hypoxic (Table 2). Physicians identified respiratory depression in only 1 of these patients. This is similar to our previous study using midazolam and fentanyl, in which blinded capnography frequently identified respiratory depression undetected by the treating physicians.<sup>7</sup> However, the true significance of these ETCO<sub>2</sub> changes in the absence of hypoxia is unclear because none of the patients in either of our studies who met only ETCO<sub>2</sub> criteria for respiratory depression had any sequelae.

Sedative hypnotics and opioids cause hypoventilation by 2 different mechanisms. Bradypneic hypoventilation, most commonly observed with opioids, occurs when respiratory rate slows more than tidal volume decreases, which produces an increase in expiratory time and an increase in ETCO<sub>2</sub>.<sup>23</sup> Six of 36 patients who met ETCO<sub>2</sub> criteria for respiratory depression had bradypneic hypoventilation (Table 3). Hypopneic hypoventilation, most often associated with sedative hypnotic use, occurs when tidal volume decreases more than respiratory rate slows, resulting in low tidal volume breathing and an increase in fractional dead space. When this occurs, ETCO<sub>2</sub> will decrease or remain normal despite an increasing PaCO<sub>2</sub>.<sup>23</sup> The majority (30 of 36) of patients in our study who met ETCO<sub>2</sub> criteria for respiratory depression had hypopneic hypoventilation (Tables 3). It is critical for physicians using sedative hypnotic agents to be familiar with these concepts because a majority of patients experiencing respiratory depression will demonstrate a decreasing ETCO<sub>2</sub> level.

It seems intuitive that depth of sedation plays an important role in the risk of respiratory depression during ED procedural sedation and analgesia. Comparison of our 2 studies evaluating supplemental oxygen seems to support this line of reasoning. In our previous study using midazolam and fentanyl, the median Ramsey score was 4, and the incidence of hypoxia was 13.9%. In the current study using propofol, the median Ramsey score was 5, and the incidence of hypoxia was 22.7%. Although these studies were not designed to determine whether respiratory depression is more dependent on the agents used or the depth of

sedation, the results do suggest that depth of sedation plays a role. We believe it would be prudent for clinicians administering procedural sedation to keep this in mind, regardless of the agent(s) being administered.

Overall, there were no significant differences in the incidence of adverse events between the 2 groups. One patient in the supplemental oxygen group received assisted ventilation after experiencing a decrease in oxygen saturation, followed by an increase in  $\text{ETCO}_2$ . We believe this reflects an acute upper airway obstruction caused by placing an obese patient in the prone position, which significantly reduced her functional residual capacity and airway compliance. This led to acute oxygen desaturation, followed over time by bradypneic hypoventilation and a gradual increase in  $\text{ETCO}_2$ .<sup>18</sup>

*Supervising editor:* Steven M. Green, MD

*Author contributions:* KD 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 provided statistical advice on study design and analyzed the data. KD drafted the article. CRC provided editorial support and contributed substantially to its revisions. KD takes responsibility for the paper as a whole.

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