CLINICAL INVESTIGATIONS

End-tidal Carbon Dioxide Monitoring during Procedural Sedation

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Abstract. Objective: To prospectively determine whether end-tidal carbon dioxide (ETCO₂) monitors can detect respiratory depression (RD) and the level of sedation in emergency department (ED) patients undergoing procedural sedation (PS). Methods: This was a prospective observational study conducted in an urban county hospital of adult patients undergoing PS. Patients were monitored for vital signs, depth of sedation per the physician by the Observer's Assessment of Alertness/Sedation scale (OAA/S), pulse oximetry, and nasal-sample ETCO₂ during PS. Respiratory depression was defined as an oxygen saturation <90%, an ETCO₂ >50 mm Hg, or an absent $ETCO_2$ waveform at any time during the procedure. The physician also determined whether protective airway reflexes were lost during the procedure and assisted ventilation was required, or whether there were any other complications. Rates of RD were compared with the physician assessment of airway loss and between agents using chi-square statistics. Spearman's rho analysis was used to determine whether there was a correlation between ETCO₂ and the OAA/S score. Results: Seventy-four patients were enrolled in the study. Forty (54.1%) received methohexital, 21 (28.4%) received propofol, ten (13.5%) re-

ceived fentanyl and midazolam, and three (4.1%) received etomidate. Respiratory depression was seen in 33 (44.6%) patients, including 47.5% of patients receiving methohexital, 19% receiving propofol (p = 0.008), 80% receiving fentanyl and midazolam, and 66.6% receiving etomidate. No correlation between OAA/S and ETCO₂ was detected. Eleven (14.9%) patients required assisted ventilation at some point during the procedure, all of whom met the criteria for RD. Pulse oximetry detected 11 of the 33 patients with RD. Post-hoc analysis revealed that all patients with RD had an ETCO₂ >50 mm Hg, an absent waveform, or an absolute change from baseline in ETCO₂ >10 mm Hg. Conclusions: There was no correlation between ETCO₂ and the OAA/S score. Using the criteria of an $ETCO_2 > 50$ mm Hg, an absolute change >10 mm Hg, or an absent waveform may detect subclinical RD not detected by pulse oximetry alone. The ETCO₂ may add to the safety of PS by quickly detecting hypoventilation during PS in the ED. Key words: sedation; monitoring; carbon dioxide; endtidal CO₂; capnography; capnometry; emergency department. ACADEMIC EMERGENCY MEDICINE 2002; 9:275-280

THE USE of procedural sedation (PS) in the emergency department (ED) has increased in frequency and scope. Procedural sedation is now routinely used for painful procedures in both adult and pediatric ED patients. Despite the increasing popularity of PS, little clinical research is available regarding its safety in the ED setting. In 1998, the American College of Emergency Physicians

(ACEP) issued a policy statement on PS, with specific recommendations about appropriate patient monitoring.¹ While noninvasive blood pressure monitors, cardiac monitors, and pulse oximetry are used extensively to monitor patients undergoing ED PS, the usefulness of these monitors has not been established. Many aspects of this technique remain understudied in the ED setting. For example, there is little information available on whether different medications used for PS require different monitoring techniques or different periods of observation.²⁻⁷ In addition, conflicting recommendations exist concerning the use of pre-oxygenation. There is evidence that pretreatment with oxygen can decrease the usefulness of pulse oximetry and mask hypoventilation, potentially delaying the appreciation of oversedation.⁸ Other unanswered questions include the depth of seda-

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accepted December 6, 2001, fevision received December 4, 2001,

Presented at the SAEM annual meeting, Atlanta, GA, May 2001.

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tion that various agents generally achieve in patients, and the effect that the depth of sedation has on the number of complications, the success of the procedure, and patient satisfaction.

Many studies have suggested that end-tidal carbon dioxide (ETCO₂) by nasal cannula is an excellent way to follow respiratory depression (RD) in PS.^{4,9-13} Some investigators believe that ETCO₂ can be used to predict the depth of sedation by measuring respiratory suppression, but to the best of our knowledge, this concept has never been compared with physician assessment of the depth of sedation, or the outcome of the procedure.^{5,10} If ETCO₂ could be shown to correlate with the depth of sedation, it would make a useful tool in further assessments of PS.

The purpose of this study was to prospectively evaluate the utility of $ETCO_2$ monitors to detect RD in patients undergoing PS. We also sought to determine whether the depth of sedation as perceived by the clinician can be predicted by the amount of RD detected by $ETCO_2$. Our hypothesis was that $ETCO_2$ is a useful monitor for detecting RD, and that it can be used to predict the level of sedation achieved. Our secondary hypothesis was that there is no difference between the rates of RD detected between the various sedative agents used in this study.

METHODS

Study Design. This was a prospective observational study of ED PS in adults using methohexital, propofol, etomidate, and fentantyl/midazolam between December 1, 2000, and April 1, 2001. The Institutional Review Board (IRB) of Hennepin County Medical Center approved this study.

Study Setting and Population. This study was performed at an urban county medical center with approximately 93,000 patient visits per year. All adult ED patients who were monitored during PS as per ED standard guidelines were eligible. In our ED, PS is commonly used for fracture and dislocation reductions, incision and drainage of abscesses, and complex laceration repair, and is at the discretion of the treating physician. The exclusion criterion was inability to give consent.

Study Protocol. Prior to the procedure, informed consent for study participation was obtained. Baseline vital signs, pulse oximetry, and ETCO₂ were recorded. The sedative agent used was recorded as well as whether the patient received pretreatment supplemental oxygen. During the procedure, pulse oximetry, heart rate, blood pressure, respiratory rate, and ETCO₂ were recorded every 2 minutes, in addition to recording the nadir. The treating physician also recorded a modified version of the OAA/S scale every 2 minutes during the procedure (Table 1).¹⁴ This scale provides a subjective measure of the patient's level of sedation. Any loss of waveform for ETCO₂ was also noted. Respiratory depression was defined as an oxygen saturation of <90% for at least 1 minute, an ETCO₂ of >50 mm Hg at any time, or airway obstruction with cessation of gas exchange at any time (noted by an absent ETCO₂ waveform). These criteria are an adaptation of criteria that have been used to define RD in previous studies using ETCO₂ in PS.^{10, 15} After the procedure the physician noted any complications and whether the patient required assisted ventilation (by bag-valve-mask) due to decreased protective airway reflexes during the procedure. The duration of any assisted ventilations was also recorded.

<u>Data Analysis.</u> Data were collected by a designated trained 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 were done using PASS and STATA (STATA Corp., College Station, TX) statistical software.

Descriptive statistics were used to determine the rates of RD detected by $ETCO_2$ and pulse oxi-

TABLE 1. The Modified* Version of the Observer's Assessment of Alertness/Sedation Scale

Responsiveness	Speech	Facial Expression	Eyes	Score
Responds readily to name spoken in normal tone	Normal	Normal	Clear, no ptosis	5
Lethargic response to name spoken in normal tone	Mild slowing or thickening	Mild relaxation	Glazed, or mild ptosis (less than half the eye)	4
Responds only after name is called loudly and repeatedly	Slurring or promi- nent slowing	Marked relaxation	Glazed and marked ptosis (half the eye or more)	3
Responds only after mild prodding or shaking	Few recognizable words	—	<u> </u>	2
Does not respond to mild prodding or shaking	—	—	—	1

*Modified with permission from: Chernik DA, Gillings D, Laine H, et al.: Validity and reliability of the Observer's Assessment of Alertness/Sedation Scale: study with intravenous midazolam. J Clin Psychopharmacol. 1990; 10:244.

metry, and the rate of RD for each sedative agent used. Rates of RD were compared between agents using chi-square statistics. The incidences of assisted ventilations in patients with and without RD were also compared using chi-square statistics. Spearman's rho analysis was used to determine whether there is an association between the Observer's Assessment of Alertness/Sedation scale (OAA/S) score and the ETCO₂. The absolute changes in ETCO₂ between the initial and the nadir between patients with OAA/S scores of <3 and those with scores of 4 or 5 were compared using a two-tailed t-test. In order to detect a 20% difference in the rate of RD between the agents using chi-square tests, with an alpha of 0.05 and a beta of 0.2 (80% power), power analysis indicated that 28 patients per sedative agent were required.

RESULTS

Seventy-four patients were enrolled in the study, with a mean age (\pm SD) of 37.6 \pm 13.4 years; 57.2% were male. Procedural sedation was used for all 74 procedures, and 72 of 74 of the procedures were successful (97.3%). The procedures performed are in listed in Table 2. No patient was noted to have adverse events other than 11 patients who required assisted ventilation (bag-valve-mask). No patient required assisted ventilation for >2minutes. The only abnormality detected by cardiac monitors was sinus tachycardia (rate >120 beats/ min), seen in six (8.1%) patients, two of whom also met criteria for RD (2.7% overall, 6.1% of patients with RD). Hypotension (blood pressure <90 mm Hg) was not detected. All patients had pulse oximetry saturations >96% prior to the procedure. Eleven patients were noted to have oxygen saturations <90% at some point in the procedure. Five of these patients had a maximum $ETCO_2$ of <50mm Hg and a normal waveform during the procedure (they did not meet the other criteria for RD). Data regarding $ETCO_2$ and pulse oximetry are summarized in Table 3. All patients had an initial OAA/S score of 5.

By our measurement criteria, RD was seen in 33 of 74 patients (age 38.8 ± 15.6 years; 56.9%were male). Seven patients met two criteria, one patient met all three criteria (Table 4). Forty-seven (64.4%) of all patients were pretreated with supplemental oxygen. Of the patients noted to have RD, 19 (57.6%) had received supplemental oxygen. Of the 11 patients noted to have an oxygen saturation <90% during the procedure, five (45.4%) had been pretreated with supplemental oxygen. In the 11 patients who were noted to have an oxygen saturation <90% at some point during the procedure, the mean nadir was 86.4 ± 4.8 years, range 78 to 90%). The only complications noted were in 11 pa-

TABLE 2. The Procedures Performed

Procedure	Number of Patients $(n = 74)$
Fracture reduction	26
Dislocation reduction	20
Incision and drainage of abscess	22
Thoracostomy tube placement	2
Hernia reduction	2
Cardioversion	1
Complex laceration repair	1

TABLE 3. End Tidal Carbon Dioxide $(ETCO_2)$ and Pulse Oximetry Values

	Mean	95% CI	Range
Oxygen saturation (%)			
Baseline	98.4	96.8, 58.3	96 - 100
Lowest	96.1	83.5, 100	78 - 100
ETCO ₂ (mm Hg)			
Baseline	42.4	26.5, 58.3	15 - 55
Highest	48.9	35.0, 62.8	24 - 63
Lowest	35.9	17.5, 54.3	9-54
Maximum absolute			
change from			
baseline	9.37	0, 24.2	0-46

 TABLE 4. Patients Meeting Criteria for Respiratory

 Depression (RD)

RD Criteria	Patients Meeting at Least One Criterion for RD $(n = 33)$	% of Total Patients (n = 74)
ETCO ₂ * >50 mm Hg Absent ETCO ₂ waveform Oxygen saturation <90%	24 (72.7%) 11 (33.3%) 11 (33.3%)	$32.4\%\ 14.9\%\ 14.9\%$

* $ETCO_2$ = end-tidal carbon dioxide.

TABLE 5. Respiratory Depression (RD) by Agent

Agent	Total $(n - 74)$	RD (n - 33)	No RD $(n - 41)$	Rate of RD
Methohexital	40 (54.1%)	19	21	47.5%
Propofol	21 (28.4%)	4	19	19%
Fentanyl/midazolam	$10\ (13.5\%)$	8	2	80%
Etomidate	3(4.1%)	2	1	66.6%

tients who required assisted ventilation (bag–valve–mask) at some point during the procedure. All 11 of these patients met our criteria for RD. Seven of the 11 had an absent ETCO₂ waveform, two had an oxygen saturation less than 90%, and two had an ETCO₂ >50 mm Hg.

The medications used for PS and the rates of RD are noted in Table 5. The rates of RD between methohexital (47.5%) and propofol (19%) were significantly different (p = 0.008). The rates of RD for

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TABLE 6.	End-tidal Carbo	ı Dioxide	$(ETCO_2)$	Changes	Based
on Pretest	Criteria: Post-ho	c Analysi	s		

RD* Criteria	Absolute Change in ETCO ₂ from Baseline (95% CI)	p-value
All patients $(n = 74)$	7.18 (4.93, 9.43)	
(n = 24) ETCO ₂ <50 mm Hg but:	11.3 (10.0. 12.6)	0.008
Absent ETCO ₂ waveform (n = 4)	18.1 (10.2, 26)	0.003
Oxygen saturation $<90\%$ ($n = 5$)	19.2 (11.1, 25.2)	0.002

*RD = respiratory depression.

fentanyl/midazolam (80%) and etomidate (66.6%) were higher than those for the other medications, but there were too few of these cases to allow a meaningful analysis, as required by our power analysis.

Table 6 shows the absolute changes (positive or negative) in ETCO₂ for all patients and in those who met our criteria for RD. Twenty-one of the 33 patients with RD had an absolute change from baseline ETCO₂ of >10 mm Hg, including all of the patients with RD who did not have a ETCO₂ >50 mm Hg. Thirty-three patients overall had a change in ETCO₂ >10 mm Hg, 21 (63.6%) of whom had RD. Of the 41 patients without RD, 12 (29.3%) had an absolute change in ETCO₂ >10 mm Hg.

No correlation between $ETCO_2$ and OAA/S score was detected by Spearman's rho analysis. Patients with a minimum OAA/S score of 4 or 5 had a mean absolute change in $ETCO_2$ of 6.63 mm Hg (95% CI = 4.23 to 9.03) vs. 9.35 mm Hg (95% CI = 8.63 to 10.07) for those with an OAA/S score of <3 (p = 0.17). Nineteen of 33 patients with detected RD never had an OAA/S score of <5.

DISCUSSION

In our series of patients undergoing PS, subclinical RD occurred frequently. The ETCO₂ monitor detected patients who met our criteria for RD who were not detected by pulse oximetry. Using the criteria of an absent ETCO₂ waveform, an ETCO₂ >50 mm Hg, or an absolute change in ETCO₂ \geq 10 mm Hg, ETCO₂ detected all episodes of RD. Propofol caused significantly less RD than the other agents (p = 0.008).

As seen in Table 7, 44.6% of patients had an absolute change from baseline ETCO_2 of >10 mm Hg, 21 (63.6%) of whom had RD. Because the numbers of false negatives and false positives for these criteria were found to be equal, the sensitivity and positive predictive value for RD of a change in ETCO_2 >10 mm Hg are 63.6%, and the specificity and negative predictive value are 70.7%.

No correlation between the ETCO_2 and the OAA/S score was detected. Although a trend toward a larger absolute change in ETCO_2 was present in patients with OAA/S scores of 3 than in patients with scores of 4 or 5, the difference was not statistically significant.

Assisted ventilation was required in 11 patients in this study. While none of these patients suffered any detectable morbidity from their RD or the assisted ventilation, it is clearly undesirable in ED PS. All of the patients who required assisted ventilation met the criteria for RD used in our study. The incidence of assisted ventilation overall (14.86%) was lower than the incidence among patients who met criteria for RD (33.33%; 95% CI = 13.63% to 53.03%, p = 0.001). This indicates that these RD criteria may detect patients at risk for developing airway complications.

End-tidal CO_2 has been used in multiple previous studies as a monitor of respiratory suppression. Hart et al. evaluated the respiratory effects of three regimens: fentanyl, fentanyl-midazolam, meperidine-promethazine-chlorpromazine. and Respiratory depression was defined as an oxygen saturation <90% for 1 minute or an ETCO₂ >50mm Hg. Rates of RD were 20%, 23%, and 11%, respectively.¹⁵ End-tidal CO₂ was more recently used by Tobias to monitor RD in 50 children who received midazolam and ketamine. In the study, RD was defined as a decreased oxygen saturation >3%from baseline, ETCO₂ >50 mm Hg, or airway obstruction with cessation of gas exchange. Only three patients met any of these criteria and there was no significant morbidity noted.¹⁰ In a study by Abramo et al., patients with seizures were monitored with ETCO₂. Those patients with decreased oxygen saturation had their oxygenation improved with supplemental oxygen, but the increased $ETCO_2$ persisted, despite the correction in oxygen saturation.¹⁶ This may indicate that patients who are already receiving supplemental oxygen could have a normal oxygenation but an elevated partial pressure of CO_2 in alveolar gas (PaCO₂) from hypoventilation. While it is not clear whether this is clinically important, PS is usually done with multiple boluses of medication, and RD is an indication that no further medication should be given. If a patient is receiving supplemental oxygen, a pulse oximeter may not be able to detect subclinical RD, and $ETCO_2$ would be a more sensitive monitor of RD. Rising ETCO₂ indicates hypoventilation, whereas hypoxia is a relatively late finding, especially in a patient receiving supplemental oxygen. Detecting hypoventilation before hypoxia develops would allow the clinician to intervene by stimulating the patient, evaluating the airway, and/or withholding additional sedatives.

Nasal-cannula ETCO₂ values correlate well

with PaCO₂ in awake, spontaneously breathing patients and may be as accurate as those measured from an endotracheal tube.8,9,11,17-21 Several studies have shown ETCO₂ to accurately detect airway obstruction.^{10, 11, 15, 22} In a study by Wright, patients who underwent conscious sedation were monitored by both pulse oximetry and ETCO₂ through nasal cannulae. It was found that values rose in all patients after sedative agents were administered, and returned to baseline during subsequent observation. Of the patients found to have a decrease in oxygen saturation, all had simultaneous rises in the $ETCO_2$ value, and the respiratory pattern noted on the monitor was slow and irregular. Clinicians queried in this study believed that the most beneficial effect of the monitor was the ability to immediately detect changes in the respiratory pattern with a glance at the capnographic waveform.⁹ End-tidal carbon dioxide by nasal cannula is not altered by concomitant oxygen administration.^{16, 17}

Pulse oximetry is the standard of care in respiratory monitoring of patients undergoing PS.^{9,23} While pulse oximetry is a sensitive monitor of arterial desaturation, it does not monitor ventilation, especially when supplemental oxygen is administered. Large changes in the partial arterial oxygen tension (PaO_2) can occur before they are detected by pulse oximetry, especially when the PaO_2 is high. Healthy patients, however, show a linear relationship between ETCO₂ and PaCO₂. This allows pulse oximetry to detect changes in the ventilatory status as they occur, and to predict the magnitude of the changes. In our study, we found that some patients who met criteria for RD showed no increase in ETCO₂. This group, however, all showed an absence of ETCO₂ waveform or a large (>10 mm Hg) absolute change in the $ETCO_2$. Since it is known that the ETCO₂ monitor does not accurately predict PaCO₂ in the presence of airway obstruction, it is likely that a large decrease from baseline demonstrates increasing airway obstruction,¹⁹ which could indicate impending airway compromise. The monitor's inability to measure the $ETCO_2$ accurately in the presence of airway obstruction can therefore be used to detect airway obstruction. A large increase from baseline should indicate a rising PaCO₂ and hypoventilation without obstruction. An absent or decreasing waveform on the monitor likewise will display worsening hypoventilation. Detecting the presence or absence of expired carbon dioxide can provide a very timesensitive picture for the clinician as to the ongoing changes in a patient's respiratory status. This information can be very useful, especially when medications are given in multiple boluses, where immediate and sensitive data regarding a patient's respiratory status can be used to assess the safety

TABLE 7. Absolute Change in ETCO₂

Respiratory	Change in ETC	Change in $ETCO_2 > 10 \text{ mm Hg}$		
Depression	Yes	No	Total	
Yes	21	12	33	
No	12	29	41	
TOTAL	33	41	74	

of a repeat bolus of medicine in an inadequately sedated patient.

LIMITATIONS AND FUTURE QUESTIONS

The primary limitation of this study is the relatively small sample size. Since complications tend to be very rare among patients undergoing PS in the ED, comparing complication rates between the two different monitors will require a large number of patients. Because of this, we adopted very sensitive criteria for RD, which more likely indicate impending RD and early hypoventilation rather than clinically significant RD.

Because this was an observational study, there were no controls and it is difficult to draw too many conclusions about the difference in the RD rates of the various agents. Randomized trials of the agents included in this study will be necessary to determine the true difference in their rates of RD. The results, however, do indicate that there may be a difference in the amount of respiratory depression associated with the various agents.

This observational study prompts several new questions: First, are patients monitored by pulse oximetry alone more likely to get an additional dose of medicine in the face of impending undetected hypoventilation, resulting in more patients' being oversedated with its associated complications? Second, is hypoventilation, as detected by an $ETCO_2$ monitor, evidence that a patient has been adequately sedated for a procedure? Third, would adding $ETCO_2$ to standard monitors result in fewer complications? Last, is pulse oximetry necessary when $ETCO_2$ is being monitored and the patient's ventilatory status is known?

CONCLUSIONS

End-tidal CO_2 does not appear to predict the level of sedation in patients undergoing ED PS. When the criteria of an ETCO₂ >50 mm Hg, an absolute change >10 mm Hg, or an absent waveform were applied, all RD was detected, regardless of the oxygen saturation. The ETCO₂ may represent an additional monitor that can add to the safety of PS by quickly detecting hypoventilation in the ED, allowing appropriate actions to be taken sooner. Differences in the rates of RD among agents were detected.

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