Capnography for Procedural Sedation and Analgesia in the Emergency Department

Baruch Krauss, MD, EdM
Dean R. Hess, RRT, PhD

From the Division of Emergency Medicine, Children's Hospital (Krauss); and the Division of Respiratory Care, Massachusetts General Hospital (Hess), Harvard Medical School (Hess, Krauss), Boston, MA.

Although it is standard of care for patient safety monitoring in anesthesia, capnography is not routinely used for emergency department procedural sedation and analgesia. We discuss the use of capnography as a diagnostic monitoring modality for procedural sedation and analgesia, focusing on the physiology and interpretation of the CO_2 waveform and recognition of normal, abnormal, and drug-induced ventilatory patterns. [Ann Emerg Med. 2007;50:172-181.]

0196-0644/$-see front matter

doi:10.1016/j.annemergmed.2006.10.016

INTRODUCTION

Procedural sedation and analgesia is the standard of care for the management of acute procedural pain and anxiety in the emergency department (ED).[1] Patient safety monitoring during ED procedural sedation and analgesia currently includes pulse rate, blood pressure, respiratory rate, oxygen saturation, ECG, and clinical observation. Noninvasive monitoring of ventilation with capnography has been studied as a research tool but is not part of routine procedural sedation and analgesia monitoring. Although standard practice in anesthesia, the use of capnography in emergency medicine has primarily been limited to intubated patients for verification of endotracheal tube placement and for cardiac arrest. There has been little emphasis on the use of capnography for assessing ventilatory status and on waveform interpretation in spontaneously breathing patients.

Capnography is a well-studied technology in anesthesia and has been used in the operating room for more than 35 years.[2,3] Anesthesiologists and respiratory physiologists began using capnography as a research tool in the 1950s. Modern capnography was developed in the 1940s by Luft[4] and commercialized in the 1960s and 1970s after the development of mass spectroscopy. Through the pioneering work of Smalhout and Kalenda,[2] capnography became a routine part of anesthesia practice in Europe in the 1970s and in the United States in the 1980s. In 1999, the American Society of Anesthesiologists issued *Standards for Basic Anesthetic Monitoring*,[5] delineating the role of capnography for all patients receiving general anesthesia: "Every patient receiving general anesthesia shall have the adequacy of ventilation continually evaluated. Qualitative clinical signs such as chest excursion, observation of the reservoir breathing bag and auscultation of breath sounds are useful. Continual monitoring for the presence of expired carbon dioxide shall be performed unless invalidated by the nature of the patient, procedure or equipment."

Capnography provides continuous, real-time, breath-to-breath feedback on the clinical status of the patient and allows the clinician to determine the baseline ventilatory status and track changes over time.[3,6] Capnography, like ECG, is a diagnostic monitoring modality because changes in the shape of the waveform are diagnostic of disease conditions.[2,3] This article discusses the use of capnography as a diagnostic monitoring tool for procedural sedation and analgesia, focusing on the physiology and interpretation of the CO_2 waveform and recognition of normal, abnormal, and drug-induced ventilatory patterns.

TERMINOLOGY

Capnography is the noninvasive measurement of the partial pressure of carbon dioxide in exhaled breath. The ancient Greeks believed there was a combustion engine inside the body that gave off smoke (*capnos* in Greek) in the form of the breath. A capnometer is a CO_2 monitor that displays a number (ie, end-tidal CO_2 [$ETCO_2$]). A capnograph is a CO_2 monitor that displays a number and a waveform. The CO_2 waveform or capnogram displays changes in the CO_2 concentration during the respiratory cycle. Carbon dioxide measured at the airway can be displayed as a function of time (CO_2 concentration over time) or exhaled tidal volume (CO_2 concentration over volume). This article will discuss the use of time-based capnography for procedural sedation and analgesia. A discussion of volume-based capnography is beyond the scope of this article. Moreover, because of certain technology characteristics, volume-based capnography is not easily adaptable to nonintubated subjects.

TECHNOLOGY

Most capnography technology is built on infrared radiation techniques. These techniques are based on the fact that CO_2 molecules absorb infrared radiation at a very specific wavelength (4.26 μm), with the amount of radiation absorbed having a close to exponential relation to the CO_2 concentration present in the breath sample. Detecting these changes in infrared radiation levels, using appropriate photodetectors sensitive in this spectral region, allows for the calculation of the CO_2 concentration in the gas sample.

Carbon dioxide monitors are designed in mainstream or sidestream configurations. Mainstream devices measure CO_2 directly from the airway, with the sensor located on the endotracheal tube. Sidestream devices measure CO_2 by aspirating a small sample from the exhaled breath through tubing to a sensor located inside the monitor. Mainstream systems, because the sensor is located on the endotracheal tube, are configured for intubated patients. Sidestream systems, because the sensor is located inside the monitor, are configured for both intubated and nonintubated patients. The airway interface for intubated patients is an airway adapter placed between the ventilator circuit and the endotracheal tube. For nonintubated patients, a nasal-oral cannula is used that allows concomitant CO_2 sampling and low-flow oxygen delivery.

Carbon dioxide monitors can either be quantitative or qualitative. Quantitative devices measure the precise $ETCO_2$ either as a number or a number and a waveform. Qualitative devices measure a range in which the $ETCO_2$ falls (eg, 0 to 10 mm Hg, >35 mm Hg) as opposed to a precise value (eg, 38 mm Hg). The predominant qualitative capnometric device is the colorimetric $ETCO_2$ detector. This device consists of a piece of specially treated litmus paper that turns color when exposed to CO_2. Its primary use is for verification of endotracheal tube placement and position. If the tube is in the trachea, the resultant exhalation of CO_2 will change the color of the litmus paper, whereas the tube in the esophagus with no CO_2 in the breath will result in no color change.

EMERGENCY MEDICINE STUDIES ON CAPNOGRAPHY USE IN PROCEDURAL SEDATION AND ANALGESIA

Research on the use of capnography for ED procedural sedation and analgesia has shown that capnography can frequently identify respiratory depression and airway complications before clinical observation.

The first ED study investigating the use of capnography for procedural sedation and analgesia was reported by Wright[7] in 1991. He studied the use of noninvasive oxygenation monitoring with pulse oximetry and noninvasive ventilation monitoring with capnography in a convenience sample of 27 adult patients undergoing procedural sedation and analgesia and found that the $ETCO_2$ increased with drug administration (fentanyl and midazolam or diazepam) and returned to baseline during recovery. The average $ETCO_2$ increase was 7 mm Hg, from an average of 35 to 42 mm Hg (average oxygen saturation decreased from 98% to 94%). Physicians and nurses were not blinded to capnography, and no definition of respiratory depression was given. Patients did not receive supplemental oxygen during sedation.

In 1997, Hart et al[8] studied the incidence of respiratory depression during procedural sedation and analgesia in a convenience sample of 42 children receiving intravenous fentanyl and midazolam or intramuscular meperidine, promethazine, chlorpromazine compound. Respiratory depression was defined as SpO_2 less than or equal to 90% for greater than 1 minute or $ETCO_2$ greater than or equal to 50 mm Hg. Respiratory depression occurred in 8 of 42 (19%) patients. Of these 8 patients, 6 had $ETCO_2$ greater than 50 mm Hg without hypoxemia and 2 had $ETCO_2$ greater than 50 mm Hg with SpO_2 less than or equal to 90. Clinicians were not blinded to capnography results.

Miner et al[9-11] conducted 3 studies between 2001 and 2003, using capnography to detect the presence of respiratory depression during ED procedural sedation and analgesia. Respiratory depression was defined as SpO_2 less than 90%, $ETCO_2$ greater than 50 mm Hg, an absolute change in $ETCO_2$ greater than 10 mm Hg, or loss of the capnogram. This expanded definition of respiratory depression was able to identify ventilatory abnormalities with both low and high $ETCO_2$, whereas previous studies were designed to capture ventilatory abnormalities with high $ETCO_2$ only (see section on drug-induced hypoventilation for further discussion of the types of hypoventilation).

In the first study, respiratory depression occurred in 33 of 74 (45%) patients using methohexital, fentanyl and midazolam, propofol, or etomidate.[9] In the second study, respiratory depression occurred in 44 of 108 (41%) patients using methohexital, fentanyl and midazolam, propofol, or etomidate.[10] In the third study, respiratory depression occurred in 50 of 103 (48%) patients using methohexital or propofol.[11] Subclinical respiratory depression occurred in 41% to 48% of patients in the 3 studies, and capnography identified patients with respiratory depression undetected by pulse oximetry. As expected (see section on drug-induced hypoventilation), subclinical respiratory depression detected by capnographic changes was not always associated with oxygen desaturation.

In 2006, Burton et al[12] investigated the temporal relationship between changes in capnography and pulse oximetry in the detection of acute respiratory events during ED procedural sedation and analgesia in a convenience sample of 59 patients and 60 sedations. The clinical team performing the sedation/procedure was blinded to capnography monitoring (because capnography was not standard monitoring practice in this institution). Respiratory depression was defined as an acute respiratory event when there was a change in $ETCO_2$ greater than or equal to 10 mm Hg from presedation baseline or an $ETCO_2$ level less than or equal to 30 mm Hg or greater than or equal to 50 mm Hg during the sedation. Acute respiratory events were

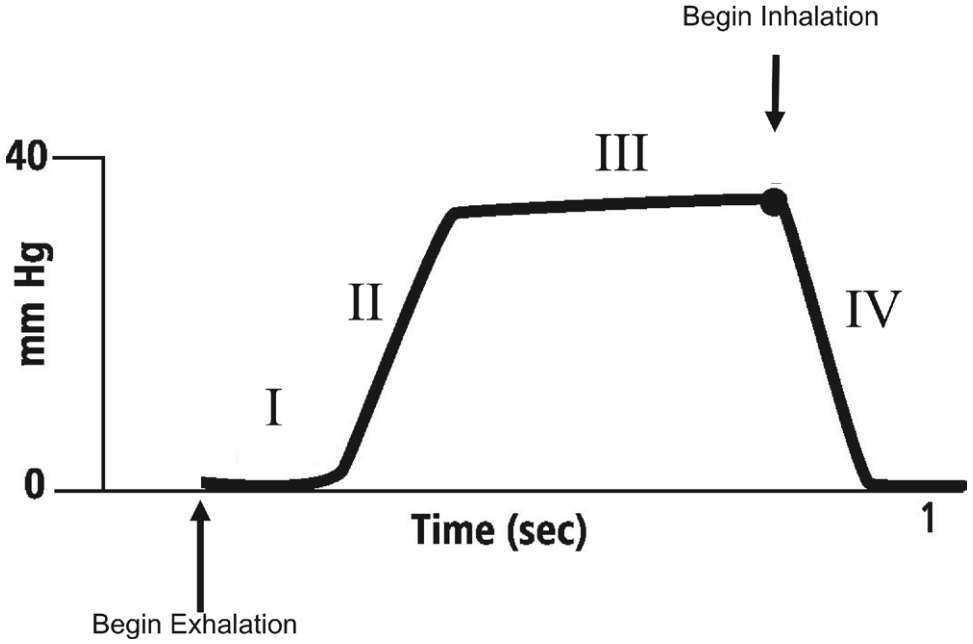


Figure 1. Normal capnogram.

detected in 20 of 60 (33%) patients. In 14 of these 20 patients (70%), capnographic changes occurred 12 to 271 seconds before changes in oxygen saturation or respiratory rate. As expected (see section on drug-induced hypoventilation), capnographic changes were not always associated with oxygen desaturation or acute interventions. Further, in approximately 50% of the capnographic changes, the $ETCO_2$ decreased in the presence of respiratory depression (see section on drug-induced hypoventilation for discussion of the significance of decreased $ETCO_2$ during hypoventilation).

Although these studies were able to develop a preliminary definition of respiratory depression and demonstrate that changes in $ETCO_2$ consistent with hypoventilation occur frequently, many questions require further investigation.

- What is the clinical significance of an increased $ETCO_2$ during procedural sedation and analgesia?
- What is the significance of an increased $ETCO_2$ without hypoxemia?
- What is the significance of a decreased $ETCO_2$ in the absence of upper airway obstruction?
- What is the clinical significance of respiratory depression as defined in these studies, especially if "subclinical" respiratory depression did not lead to an adverse event?
- Is there an $ETCO_2$ threshold or range associated with airway interventions? With significant oxygen desaturation ($\leq$90%)? With respiratory failure? With apnea? With ineffective ventilation?
- Does the use of capnography decrease the incidence of hypoxemia during procedural sedation and analgesia?
- Does the use of capnography decrease the number of clinical interventions for acute respiratory events during procedural sedation and analgesia?

PHYSIOLOGY

The capnogram, corresponding to a single tidal breath, has been described as having 4 phases (ascending phase, alveolar plateau, inspiratory limb, dead space ventilation) in which each of these phases has conventionally been approximated as a straight line.[2,13] Thus, the capnogram of a subject with normal lung function, irrespective of age, has been described as rectangular or trapezoidal. At the start of exhalation, the concentration of CO_2 is initially zero (phase I) as the airway dead space is exhaled and then increases rapidly as alveolar gas exits the airway (phase II). For most of exhalation, CO_2 concentration is relatively constant and reflects the concentration of CO_2 in the alveolar gas (phase III). This phase concludes with a point of maximum CO_2 concentration at the $ETCO_2$ value. With the start of inhalation (phase IV), the CO_2 concentration decreases to zero as atmospheric air enters the airway (Figure 1).

A normal capnogram for patients of all ages is characterized by a set of specific elements: it includes 4 distinct phases (Figure 1), the CO_2 concentration starts at zero and returns to zero (ie, there is no rebreathing of CO_2), a maximum CO_2 concentration is reached with each breath (ie, $ETCO_2$), the amplitude depends on the $ETCO_2$ concentration, the width depends on the expiratory time, and there is a characteristic shape for all subjects with normal lung function.

The capnogram is traditionally interpreted by visual inspection, with qualitative pattern recognition consisting of a set of abnormal capnogram results and a corresponding differential diagnosis for each abnormal shape.[2,3,14,15] Although waveform analysis (which will be discussed in greater detail in the next section) is a useful diagnostic tool, it has limitations as a waveform that has not been quantified. Pattern recognition is adequate for situations in which assessment is based on the presence or absence of the capnogram (verification of endotracheal tube placement, apnea, upper airway obstruction, laryngospasm),[3,16-18] and in which the abnormal capnogram shape is characteristic of a specific condition or disease entity (obstructive lung disease/bronchospasm, hypoventilation, hyperventilation).[19-24] Although the naked eye can discern gross changes in waveform amplitude and shape, it cannot recognize small yet diagnostically significant changes in the angles and slopes of segments of the capnogram. Without the ability to discern minor gradations in shape, capnogram results may only be categorized as normal or abnormal. The ECG has been characterized by a standard suite of amplitude and interval measurements, facilitating quantitative research and physician- and computer-based interpretation. Similar quantitative characterization of the capnogram is needed to maximize its utility as a diagnostic tool.

The majority of patients undergoing procedural sedation and analgesia will have normal lung function, and therefore the P(a-et)CO_2 gradient will be narrow (0 to 5 mm Hg), with the $ETCO_2$ accurately reflecting the $PaCO_2$.[25] In patients with abnormal lung function, the gradient will widen, depending on the severity of the lung disease, and the $ETCO_2$ will be useful only for assessing trends ventilatory status over time and not as a single-number spot check that may or may not correlate with the $PaCO_2$.[26,27] An increased P(a-et)CO_2 is the result of dead space, and a decrease in tidal volume increases dead space fraction and the P(a-et)CO_2 gradient (see section on drug-induced hypoventilation).[26,27]

CAPNOGRAPHIC ASSESSMENT OF VENTILATORY PATTERNS DURING PROCEDURAL SEDATION AND ANALGESIA

Capnography is the only single monitoring modality that provides airway, breathing, and circulation assessment.[6] The presence of a normal waveform denotes that the airway is patent and that the patient is breathing. Normal $ETCO_2$ (35 to 45 mm Hg), in the absence of obstructive lung disease, reflects adequate perfusion. Unlike pulse oximetry, the capnogram remains stable during patient motion and is reliable in low-perfusion states. Capnography is the earliest indicator of airway or respiratory compromise and can rapidly identify the common adverse events associated with procedural sedation and analgesia including apnea, upper airway obstruction, laryngospasm, bronchospasm, and respiratory failure (Table 1).[12,24,28-36]

Definition of Respiratory Depression

Respiratory depression causes a reduction in alveolar ventilation by a decrease in respiratory rate or tidal volume caused by a decrease in respiratory drive. The result is an increase in $PaCO_2$.[37] By definition, hypoventilation is arterial hypercarbia ("a state in which there is a reduced amount of air entering the pulmonary alveoli [decreased alveolar ventilation], resulting in increased carbon dioxide tension").[38] One cannot diagnose hypoventilation, and hence respiratory depression, without some measure of alveolar or arterial CO_2.

Normal Ventilatory Patterns

Normal, Hyperventilation, and Hypoventilation Patterns. Changes in $ETCO_2$ and expiratory time affect the shape of the capnogram.[2,5,14,39] The amplitude of the capnogram is determined by $ETCO_2$, and the width is determined by the expiratory time. Hyperventilation (increased respiratory rate, decreased $ETCO_2$) results in a low amplitude and narrow capnogram, whereas classic hypoventilation (decreased respiratory rate, increased $ETCO_2$) results in a high amplitude and wide capnogram (Table 1).[2,4,14,39]

Physiological Variability. Unlike other types of vital sign monitoring during procedural sedation and analgesia (pulse rate, blood pressure, SpO_2), there can be considerable breath-to-breath variability in the shape and size of the capnogram in normal, nonsedated subjects (Table 1).[2,15,37] This physiologic variability results from normal variations in ventilatory pattern that occur during talking (long and short breaths, slow and fast/rapid breathing) and anxiety states (especially preprocedural anxiety) and in young children. Ventilatory pattern stabilizes and physiologic variability decreases as the depth of sedation increases.[40]

Drug-Induced Ventilatory Patterns

There are 7 primary drug-induced ventilatory patterns that can occur with procedural sedation and analgesia: periodic breathing, apnea, upper airway obstruction, laryngospasm, bronchospasm, hypoventilation, and respiratory failure.

Periodic Breathing. Periodic breathing is characterized by normal breathing punctuated with apneic pauses, occurring most commonly during deep sedation (Table 1).[2,15,37,39] This pattern may be self-resolving or devolve into complete central apnea.[2,15,37,40]

Apnea. Apnea can be almost instantaneously detected by capnography. Loss of the capnogram, the earliest indicator of cessation of ventilation, in conjunction with no chest wall movement and no breath sounds on auscultation, confirms the diagnosis of central apnea (Table 1).[2,4,40]

Capnography may be more sensitive than clinical assessment of ventilation in detection of apnea.[12,29,34-36] In a recent study,

Table 1. Capnographic airway assessment for procedural sedation and analgesia.

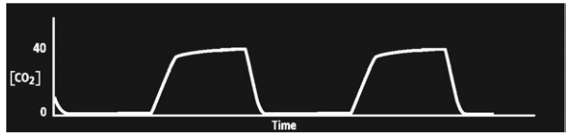
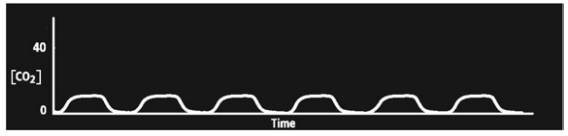
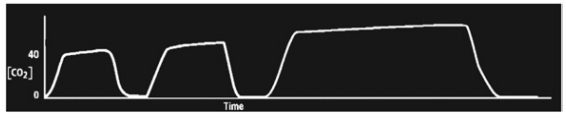
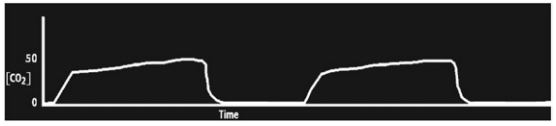
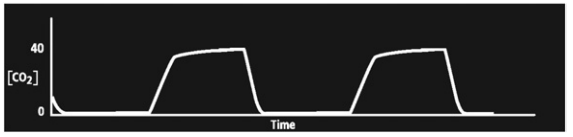
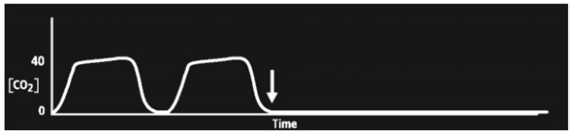
Diagnosis	Waveform	Features		Intervention
Normal		SpO_2 $ETCO_2$ Waveform RR	normal normal normal normal	No intervention required Continue sedation
Hyperventilation		SpO_2 $ETCO_2$ Waveform RR	normal ↓ decreased amplitude and width ↑	
Bradypneic Hypoventilation (Type 1)		SpO_2 $ETCO_2$ Waveform RR	normal ↑ increased amplitude and width ↓ ↓ ↓	Reassess patient Continue sedation
		SpO_2 $ETCO_2$ Waveform RR	↓ ↑ increased amplitude and width ↓ ↓ ↓	Reassess patient Assess for airway obstruction Supplemental oxygen Cease drug administration or reduce dosing
Hypopneic Hypoventilation (Type 2)		SpO_2 $ETCO_2$ Waveform RR	normal ↓ decreased amplitude ↓	Reassess patient Continue sedation
		SpO_2 $ETCO_2$ Waveform RR	↓ ↓ decreased amplitude ↓	Reassess patient Assess for airway obstruction Supplemental oxygen Cease drug administration or reduce dosing
Hypopneic Hypoventilation with periodic breathing		SpO_2 $ETCO_2$ Waveform RR Other	normal or ↓ ↓ decreased amplitude ↓ apneic pauses	

Table 1. Continued

Diagnosis	Waveform	Features		Intervention	
Physiological variability		SpO_2 $ETCO_2$ Waveform RR	normal normal varying* normal	No intervention required Continue sedation	
Bronchospasm		SpO_2 $ETCO_2$ Waveform RR Other	normal or ↓ normal, ↑, or ↓† curved normal, ↑, or ↓† wheezing	Reassess patient Bronchodilator therapy Cease drug administration	
Partial airway obstruction		SpO_2 $ETCO_2$ Waveform RR Other	normal or ↓ normal normal variable noisy breathing and/or inspiratory stridor	Full airway patency restored with airway alignment Noisy breathing and stridor resolve	Reassess patient Establish IV access Supplemental O_2 (as needed) Cease drug administration
Partial laryngospasm				Airway not fully patent with airway alignment Noisy breathing and stridor persist	
Apnea		SpO_2 $ETCO_2$ Waveform RR Other	normal or ↓‡ zero absent zero no chest wall movement or breath sounds	Reassess patient Stimulation Bag mask ventilation Reversal agents (where appropriate) Cease drug administration	
Complete airway obstruction		SpO_2 $ETCO_2$ Waveform RR Other	normal or ↓‡ zero absent zero chest wall movement and breath sounds present	Airway patency restored with airway alignment Waveform present	
Complete laryngospasm				Airway not patent with airway alignment No waveform	Positive pressure ventilation

*Varying waveform amplitude and width.
†Depending on duration and severity of bronchospasm.
‡Depending on duration of episode.

Table 2. Characteristics of bradypneic (type 1) and hypopneic (type 2) hypoventilation.

Hypoventilation Type	Respiratory Rate	V_T	Airway Dead Space	V_D/V_T	$ETCO_2$	$PaCO_2$
Bradypneic (type 1)	↓ ↓ ↓	↓	Constant/no change	Minimal change	↑	↑
Hypopneic (type 2)	↓	↓ ↓ ↓	Constant/no change	↑ ↑ ↑	↓, Or no change	↑

V_D, Dead space volume; V_T, tidal volume.

Table 3. Drug-induced hypoventilation patterns.

Type	Physiology	Subtype	Features
Normal	No appreciable change in respiratory pattern		No change in respiratory rate or V_T Normal $ETCO_2$ and normal SpO_2
Mild respiratory depression	Minimal change in respiratory pattern		Minimal decrease in respiratory rate and minimal decrease in V_T Normal $ETCO_2$ Normal SpO_2
Bradypneic hypoventilation (type 1)	Hypoventilation with minimal tidal volume change Drugs that affect RR ≫ V_T	a	Decreased minute ventilation High $ETCO_2$ Normal SpO_2
		b	Decreased minute ventilation High $ETCO_2$ Decreased SpO_2
Hypopneic hypoventilation (type 2)	Hypoventilation with low tidal volume breathing	a	Decreased minute ventilation Low $ETCO_2$ and normal SpO_2
	Drugs that affect V_T ≫ RR	b	Decreased minute ventilation Low $ETCO_2$ and decreased SpO_2 Can devolve to: Intermittent apneic pauses interspersed with normal ventilation (periodic breathing) Central apnea

RR, Respiratory rate; V_T, tidal volume.

10 of 39 (26%) patients experienced 20-second periods of apnea during procedural sedation and analgesia.[29] All 10 episodes of apnea were detected by capnography but not by the anesthesia providers.

Upper Airway Obstruction. Partial upper airway obstruction can be diagnosed clinically by the presence of stridor or noisy respirations. The diagnosis of complete upper airway obstruction or obstructive apnea is based on loss of the capnogram in conjunction with 3 clinical findings: chest wall movement, no breath sounds on auscultation, and the absence of stridor or upper airway sounds.[2,14] The absence of the capnogram in association with the presence or absence of chest wall movement distinguishes apnea from upper airway obstruction and laryngospasm. Response to airway alignment maneuvers can further distinguish upper airway obstruction from laryngospasm (Table 1).[40]

Capnography also provides a nonimpedance respiratory rate directly from the airway (by oral-nasal cannula),[4] which is more accurate than impedance-based respiratory monitoring, especially in patients with complete upper airway obstruction or laryngospasm, in which impedance-based monitoring will interpret chest wall movement without ventilation as a valid breath. Although turbulence associated with partial laryngospasm affects expiratory flow, it does not affect the amplitude of the capnogram unless it results in hypoventilation or is associated with another abnormal finding such as bronchospasm.

Laryngospasm. Partial laryngospasm is detected by the presence of noisy breathing and normal oxygenation that is not relieved by airway alignment maneuvers in a previously normal subject receiving procedural sedation and analgesia agents (Table 1). The diagnosis of complete laryngospasm is based on loss of the CO_2 waveform in conjunction with 4 clinical findings: chest wall movement, no breath sounds on auscultation, absence of stridor or upper airway sounds, and no response to airway alignment maneuvers (no capnogram despite airway alignment maneuvers).[40,41]

Bronchospasm. The characteristic capnogram (curved ascending phase and upsloping alveolar plateau) observed with lower airway obstruction indicates the presence of acute bronchospasm or obstructive lung disease (Table 1).[23]

Respiratory Failure. An $ETCO_2$ greater than 70 mm Hg in patients without chronic hypoventilation indicates respiratory failure.[36,39,42]

Drug-Induced Hypoventilation

There are 2 types of hypoventilation that occur during procedural sedation and analgesia (Tables 1-3). Bradypneic hypoventilation (type 1) is characterized by an increased $ETCO_2$ and an increased $PaCO_2$. Respiratory rate is depressed

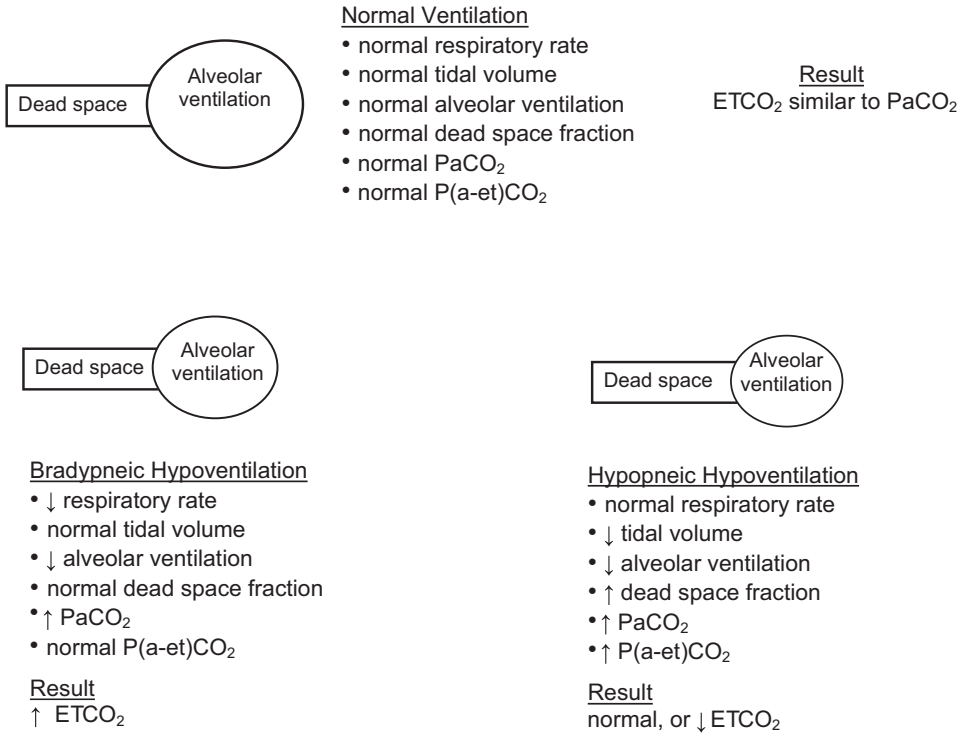


Figure 2. Physiology of hypoventilation states.

proportionally greater than tidal volume, resulting in bradypnea, an increase in expiratory time, and an increase in $ETCO_2$, graphically represented by a high amplitude and wide capnogram (Tables 1-3, Figure 2).[2,14,37,40,42] Bradypneic hypoventilation is commonly observed with opioids. Bradypneic hypoventilation (decreased respiratory rate, high amplitude, and wide capnogram) can readily be distinguished from hyperventilation (increased respiratory rate, low amplitude, and narrow capnogram; Tables 1-3; Figure 2).[2,14,15]

Hypopneic hypoventilation (type 2) is characterized by a normal or decreased $ETCO_2$ and an increased $PaCO_2$, reflecting the relationship between tidal volume and airway dead space, in which airway dead space is constant (eg, 150 mL in the normal adult lung) and tidal volume is decreasing (Tables 1-3; Figure 2). Here, tidal volume is depressed proportionally greater than respiratory rate, resulting in low tidal volume breathing that leads to an increase in airway dead-space fraction (dead-space volume/tidal volume). As tidal volume decreases, airway dead space fraction increases. The gradient between $PaCO_2$ and $ETCO_2$ increases with the increase in dead-space fraction.[26] Even though $PaCO_2$ is increasing, $ETCO_2$ may remain normal or be decreasing, which is graphically represented by a low-amplitude capnogram and occurs most commonly with sedative-hypnotic drugs (Tables 1-3; Figure 2).

It is essential for emergency physicians to understand the physiology of hypopneic hypoventilation because it occurs frequently with sedative/hypnotics and with deep sedation and can otherwise go unrecognized or misinterpreted as hyperventilation. This is presumably the mechanism for the low $ETCO_2$ reported by Burton et al[12] and Miner et al,[9-11] which occurred in about 50% of cases of respiratory depression.

Hypopneic hypoventilation follows a variable course and may remain stable, with low tidal volume breathing resolving over time as central nervous system drug levels decrease and redistribution to the periphery occurs, progress to periodic breathing with intermittent apneic pauses (which may resolve spontaneously or progress to central apnea), or progress directly to central apnea.[37,40]

Bradypneic hypoventilation follows a more predictable course, with $ETCO_2$ increasing progressively until respiratory failure and apnea occur. Although there is no absolute threshold at which apnea occurs, patients without chronic hypoventilation and with $ETCO_2$ greater than 80 mm Hg are at significant risk.[37,39]

Abnormal respiratory patterns during a single sedation event can vary in their type and severity (Tables 1-3).[1,40] Further, the onset of hypoventilation during procedural sedation and analgesia can be sudden, rapid, or gradual depending on the rapidity of central nervous system penetration and the time course of drug distribution.[40,43]

Several factors contribute to the development of hypoxia, apnea, and upper airway obstruction during ED procedural sedation and analgesia, especially during deep sedation: supine position, decreased tidal volume, and direct depression of respiratory drive. When a patient is placed in the supine position during procedural sedation and analgesia, the

abdominal viscera cause cephalad displacement of the diaphragm, decreasing functional residual capacity by 0.5 to 1 L.[44] Further reductions in functional residual capacity may result from atelectasis as a result of low tidal volume breathing in hypopneic hypoventilation.[45,46] This cumulative reduction in functional residual capacity can initiate a cascade of events that result in decreased lung compliance and airway caliber, leading to upper airway obstruction, which in turn increases airway resistance and results in a decrease in oxygenation and ultimately results in hypoxemia.[37,47]

Low tidal volume breathing increases dead-space ventilation when normal compensatory mechanisms are inhibited by drug effects. Here, minute ventilation, which normally increases to compensate for an increase in dead space, does not change or may decrease.[37] Further, as minute ventilation decreases, there is a decrease in arterial oxygenation.[48] As minute ventilation decreases further, oxygenation is further impaired.[48] However, $ETCO_2$ may initially be high (bradypneic hypoventilation) or low (hypopneic hypoventilation) without significant changes in oxygenation, particularly if the patient is breathing supplemental oxygen. We can now begin to understand why a drug-induced increase or decrease in $ETCO_2$ does not necessarily lead to oxygen desaturation and may not require intervention.

CONCLUSION

Capnography is a useful diagnostic monitoring tool for airway, breathing, and circulation assessment and rapid capnogram identification of procedural sedation and analgesia-related airway and respiratory adverse events. Further research is needed to better understand the clinical significance of changes in $ETCO_2$ levels during procedural sedation and analgesia.

Supervising editor: Richard M. Levitan, MD

Dr. Krauss is a consultant for Oridion Medical, a capnography company, and holds 2 patents in the area of capnography.

Funding and support: By *Annals* policy, all authors are required to disclose any and all commercial, financial, and other relationships in any way related to the subject of this article, that might create any potential conflict of interest. The authors have stated that no such relationships exist. See the Manuscript Submission Agreement in this issue for examples of specific conflicts covered by this statement.

Publication dates: Received for publication July 14, 2006. Revision received September 26, 2006. Accepted for publication October 23, 2006. Available online January 12, 2007.

Reprints not available from the authors.

Address for correspondence: Baruch Krauss, MD, EdM, Division of Emergency Medicine, Children's Hospital, 300 Longwood Avenue, Boston, MA 02115; 617-355-4049, fax 617-730-0335; E-mail baruch.krauss@childrens.harvard.edu.

REFERENCES

1. Krauss B, Green SM. Procedural sedation and analgesia in children. *Lancet*. 2006;367:766-780.
2. Smalhout B, Kalenda Z. *An Atlas of Capnography*. Utrecht, The Netherlands: Kerckebusch-Zeist; 1975.
3. Swedlow DB. Capnometry and capnography: the anesthesia disaster early warning system. *Semin Anesth*. 1986;3:194-205.
4. Gravenstein JS, Jaffe MB, Paulus DA, eds. *Capnography: Clinical Aspects*. Cambridge, England: Cambridge University Press; 2004.
5. American Society of Anesthesiologists. Standards for basic anesthetic monitoring: approved October 21, 1986 and last amended October 25, 2005. Available at: http://www.asahq.org/publicationsAndServices/standards/02.pdf. Accessed August 6, 2006.
6. Krauss B. Capnography as a rapid assessment and triage tool for chemical terrorism. *Pediatr Emerg Med*. 2005;21:493-497.
7. Wright SW. Conscious sedation in the emergency department: the value of capnography and pulse oximetry. *Ann Emerg Med*. 1992; 21:551-555.
8. Hart LS, Berns SD, Houck CS, et al. The value of end-tidal CO_2 monitoring when comparing three methods of procedural sedation for children undergoing painful procedures in the emergency department. *Pediatr Emerg Care*. 1997;13:189-193.
9. Miner JR, Heegaard W, Plummer D. End-tidal carbon dioxide monitoring during procedural sedation. *Acad Emerg Med*. 2002;9: 275-280.
10. Miner JR, Biros M, Heegaard W, et al. Bispectral EEG analysis of patients undergoing procedural sedation in the emergency department. *Acad Emerg Med*. 2003;10:638-643.
11. Miner JR, Biros M, Krieg S, et al. Randomized clinical trial of propofol versus methohexital for procedural sedation during fracture and dislocation reduction in the emergency department. *Acad Emerg Med*. 2003;10:931-937.
12. Burton JH, Harrah JD, Germann CA, et al. Does end-tidal carbon dioxide monitoring detect respiratory events prior to current sedation monitoring practices? *Acad Emerg Med*. 2006;13: 500-504.
13. Berengo A, Cutillo A. Single-breath analysis of carbon dioxide concentration records. *J Appl Physiol*. 1961;16:522-530.
14. Smalhout B. *A Quick Guide to Capnography and Its Use in Differential Diagnosis*. Hewlett-Packard; 1983. Hewlett-Packard Application Note 78345-90011.
15. Kalenda Z. *Mastering Infrared Capnography*. Utrecht, The Netherlands: Kerckebusch-Zeist; 1989.
16. Cote CJ, Liu LM, Szyfelbein SK, et al. Intraoperative events diagnosed by expired carbon dioxide monitoring in children. *Can Anaesth Soc J*. 1986;33:315-320.
17. Guggenberger H, Lenz G, Federle R. Early detection of inadvertent oesophageal intubation: pulse oximetry vs. capnography. *Acta Anaesthesiol Scand*. 1989;33:112-115.
18. Vaghadia H, Jenkins LC, Ford RW. Comparison of end-tidal carbon dioxide, oxygen saturation and clinical signs for the detection of oesophageal intubation. *Can J Anaesth*. 1989;36:560-564.
19. Poppius H. Expiratory CO_2 curve in pulmonary disease. *Scand J Resp Dis*. 1969;50:135-146.
20. Smidt U. Emphysema as possible explanation for the alteration of expiratory PO_2 and PCO_2 curves. *Bull Eur Physiopathol Respir*. 1976;12:605-624.
21. Kelsey JE, Oldham EC, Horvath SM. Expiratory carbon dioxide concentration curve: a test of pulmonary function. *Dis Chest*. 1962;41:498-503.
22. You B, Peslin R, Duvivier C, et al. Expiratory capnography in asthma: evaluation of various shape indices. *Eur Respir J*. 1994;7:318-323.

23. Yaron M, Padyk P, Hutsinpiller M, et al. Utility of the expiratory capnogram in the assessment of bronchospasm. *Ann Emerg Med*. 1996;28:403-407.
24. Krauss B, Deykin A, Lam A, et al. Capnogram shape in obstructive lung disease. *Anesth Analg*. 2005;100:884-888.
25. Hoffbrand BI. The expiratory capnogram: a measure of ventilation-perfusion inequalities. *Thorax*. 1966;21:518-523.
26. Yamanaka MK, Sue DY. Comparison of arterial-end-tidal Pco_2 difference and dead space/tidal volume ratio in respiratory failure. *Chest*. 1987;92:832-835.
27. Hardman JG, Aitkenhead AR. Estimating alveolar dead space from the arterial to end-tidal CO_2 gradient: a modeling analysis. *Anesth Analg*. 2003;97:1846-1851.
28. Poirier MP, Gonzalez Del-Rey JA, McAneney CM, et al. Utility of monitoring capnography, pulse oximetry, and vital signs in the detection of airway mishaps: a hyperoxemic animal model. *Am J Emerg Med*. 1998;16:350-352.
29. Soto RG, Fu ES, Vila H, et al. Capnography accurately detects apnea during monitored anesthesia care. *Anesth Analg*. 2004;99: 379-382.
30. Vargo JJ, Zuccaro G, Dumot JA, et al. Automated graphic assessment of respiratory activity is superior to pulse oximetry and visual assessment for the detection of early respiratory depression during therapeutic upper endoscopy. *Gastrointest Endosc*. 2002;55:826-831.
31. Kaneko Y. Clinical perspectives on capnography during sedation and general anesthesia in dentistry. *Anesth Prog*. 1995;42: 126-130.
32. Croswell RJ, Dilley DC, Lucas WJ, et al. A comparison of conventional versus electronic monitoring of sedated pediatric dental patients. *Pediatr Dent*. 1995;17:332-329.
33. Tobias JD. End-tidal carbon dioxide monitoring during sedation with a combination of midazolam and ketamine for children undergoing painful, invasive procedures. *Pediatr Emerg Care*. 1999;15:173-175.
34. Weingarten M. Respiratory monitoring of carbon-dioxide and oxygen: a ten-year retrospective. *J Clin Monit*. 1990;6:217-225.
35. Muttitt SC, Finer NN, Tierney AJ, et al. Neonatal apnea: diagnosis by nurse versus computer. *Pediatrics*. 1988;82:713-720.
36. Lightdale JR, Goldmann DA, Feldman HA, et al. Microstream capnography improves patient monitoring during moderate sedation: a randomized, controlled trial. *Pediatrics*. 2006;117: 1170-1178.
37. Lumb AB. Respiratory system resistance. In: *Nunn's Applied Respiratory Physiology*. 5th ed. Oxford, England: Butterworth-Heinemann; 2000.
38. *Dorland's Illustrated Medical Dictionary*. 30th ed. Philadelphia, PA: Saunders/Elsevier Publishers; 2003.
39. Barash PG, Cullen BF, Stoelting RK, eds. *Clinical Anesthesia*. 5th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2006.
40. Roy WL, Lerman J. Laryngospasm in paediatric anesthesia. *Can J Anaesth*. 1988;35:93-98.
41. Guyton AC, Hall JE. *Textbook of Medical Physiology*. 10th ed. Philadelphia, PA: WB Saunders; 2000.
42. West JB. *Respiratory Physiology: The Essentials*. 6th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2000.
43. White PF, ed. *Textbook of Intravenous Anesthesia*. Baltimore, MD: Williams & Wilkins; 1997.
44. Craig DB, Wahba WM, Don HF, et al. "Closing volume" and its relationship to gas exchange in seated and supine positions. *J Appl Physiol*. 1971;31:717-721.
45. Huang YC, Weinmann GG, Mitzner W. Effect of tidal volume and frequency on the temporal fall in lung compliance. *J Appl Physiol*. 1988;65:2040-2045.
46. Bendixen HH, Bullwinkel B, Hedley-Whyte J, et al. Atelectasis and shunting during spontaneous ventilation in anesthetized patients. *Anesthesiology*. 1964;25:297-301.
47. Mead J, Agostoni E. Dynamics of breathing. In: *Handbook of Physiology*. Vol. 1. Fenn WO, Rahn H, eds. Baltimore, MD: Williams & Wilkins; 1964.
48. Wilson WC, Shapiro B. Perioperative hypoxia: the clinical spectrum and current oxygen monitoring methodology. *Anesthesiol Clin North Am*. 2001;19:769-812.