American College of Emergency Physicians

Clinical Policy: Procedural Sedation and Analgesia in the Emergency Department

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From the American College of Emergency Physicians Clinical Policies Subcommittee (Writing Committee) on Procedural Sedation and Analgesia

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ABSTRACT

This clinical policy from the American College of Emergency Physicians is the revision of a 2005 clinical policy evaluating critical questions related to procedural sedation in the emergency department.[1] A writing subcommittee reviewed the literature to derive evidence-based recommendations to help clinicians answer the following critical questions: (1) In patients undergoing procedural sedation and analgesia in the emergency department, does preprocedural fasting demonstrate a reduction in the risk of emesis or aspiration? (2) In patients undergoing procedural sedation and analgesia in the emergency department, does the routine use of capnography reduce the incidence of adverse respiratory events? (3) In patients undergoing procedural sedation and analgesia in the emergency department, what is the minimum number of personnel necessary to manage complications? (4) In patients undergoing procedural sedation and analgesia in the emergency department, can ketamine, propofol, etomidate, dexmedetomidine, alfentanil and remifentanil be safely administered? A literature search was performed, the evidence was graded, and recommendations were given based on the strength of the available data in the medical literature.

INTRODUCTION

Procedural sedation and analgesia is a common emergency department (ED) clinical practice that alleviates pain, anxiety, and suffering for patients during medical procedures. Effective sedation enhances the performance of these procedures, with improvements in the patient and medical provider experience. Procedural sedation involves administering sedative or dissociative agents with or without the concomitant delivery of analgesic agents.

The practice of emergency medicine requires physicians to have expertise in critical care skills, including advanced airway management, cardiovascular and ventilator resuscitation techniques, and analgesia. Expertise in procedural sedation and analgesia is included as a core competency in emergency medicine residency training, as well as pediatric emergency medicine fellowships.[2-4]

Procedural sedation and analgesia continues to be a topic that attracts a great deal of attention by policymaking entities within medical specialties, as well as regulatory agencies.[5-8] Given the frequent use of procedural sedation and analgesia by emergency physicians, as well as the continued development of research and

clinical evidence for this practice, the Clinical Policies Committee of the American College of Emergency Physicians (ACEP) has developed this revision of the previous clinical policy.[1]

Since the previous ACEP clinical policy on procedural sedation and analgesia,[1] a great deal of literature has been published addressing clinical procedural sedation and analgesia practice both within the field of emergency medicine and by other specialties. The Centers for Medicare & Medicaid Services (CMS) has issued revised hospital anesthesia services interpretive guidelines that address the broad categorization of anesthesia and analgesia while noting that the level of sedation for specific sedation agents may vary in accordance with dosing, patient selection, and route of administration.[5] This revised language is particularly helpful in light of specific short-acting sedatives, such as propofol, that have clinical use as a procedural sedation and analgesia medication outside of the operative and procedure suites. The CMS guidelines note that "for some medications there is no bright line that distinguishes when their pharmacological properties bring about the physiologic transition from the analgesic to the anesthetic effects."[5] The CMS guidelines emphasize that hospital policies must be based on nationally recognized guidelines; the source of the guidelines may include a number of specialty organizations, including ACEP. As noted by CMS: "The ED is a unique environment where patients present on an unscheduled basis with often very complex problems that may require several emergent or urgent interventions to proceed simultaneously to prevent further morbidity or mortality."[9] The unique procedural sedation and analgesia qualifications of emergency physicians are also recognized by CMS: "…emergency medicine-trained physicians have very specific skill sets to manage airways and ventilation that is necessary to provide patient rescue. Therefore, these practitioners are uniquely qualified to provide all levels of analgesia/sedation and anesthesia (moderate to deep to general)."[9]

Critical questions relevant to the current practice of emergency medicine were developed for this revision, which addresses these critical questions in addition to offering a summary of recent concepts, agents, and developments in procedural sedation and analgesia.

DEFINITIONS

Procedural sedation should be viewed as a treatment strategy for the administration of sedative or analgesic medications to intentionally suppress a patient's level of consciousness. The intended sedation depth

should vary in accordance with the specific needs of the patient and procedure. Sedation depths of "mild," "moderate," and "deep" levels of altered consciousness are frequently cited in the medical literature. These descriptors should be visualized as depressed levels of consciousness along a continuum of sedation that leads to general anesthesia. This clinical policy includes items classified by CMS as anesthesia services including sedation and anesthesia.[5]

Procedural sedation and analgesia: Procedural sedation and analgesia refers to the technique of administering sedatives or dissociative agents with or without analgesics to induce an altered state of consciousness that allows the patient to tolerate painful or unpleasant procedures while preserving cardiorespiratory function.[1] The intent of the sedation, not necessarily the agent itself, determines whether medication is being delivered to relieve anxiety (anxiolysis) or to facilitate a specific procedure as with procedural sedation.

Minimal sedation: Minimal sedation describes a patient with a near-baseline level of alertness, a pharmacologically induced state during which patients respond normally to verbal commands. Although cognitive function and coordination might be impaired, ventilatory and cardiovascular functions are unaffected.[5,10] In the ED, minimal sedation is commonly administered to facilitate minor procedures.

Moderate sedation: Moderate sedation is a pharmacologically induced depression of consciousness during which patients respond purposefully to verbal commands, either alone or accompanied by light tactile stimulation. No interventions are required to maintain a patent airway, and spontaneous ventilation is adequate. Cardiovascular function is usually maintained.[1,5,10] Moderate-sedation patients often exhibit eyelid ptosis, slurred speech, and delayed or altered responses to verbal stimuli. Event amnesia will frequently occur under moderate sedation levels. In the ED, moderate sedation is commonly achieved with a benzodiazepine, often in conjunction with an opioid such as fentanyl.

Dissociative sedation: Dissociative sedation is a trance like cataleptic state characterized by profound analgesia and amnesia, with retention of protective airway reflexes, spontaneous respirations, and cardiopulmonary stability.[1,11] In the ED, ketamine is commonly administered to evoke dissociative levels of

sedation. Dissociative state can facilitate moderate to severely painful procedures, as well as procedures requiring immobilization in uncooperative patients.

Deep sedation: Deep sedation is a pharmacologically induced depression of consciousness during which patients cannot be easily aroused but respond purposefully after repeated or painful stimulation. The ability to independently maintain ventilatory function may be impaired. Patients may require assistance in maintaining a patent airway and spontaneous ventilation may be inadequate. Cardiovascular function is usually maintained.[1,5,10] Monitoring for deep sedation encounters should emphasize the potential for reduction in ventilation and cardiovascular complications, including changes to pulse rate, heart rhythm, and blood pressure.

Deep sedation is commonly achieved with short-acting sedative agents such as propofol, etomidate, or a benzodiazepine. For painful procedures, an opioid such as fentanyl or morphine sulfate may be used in concert with the sedative. Many recent studies have described the use of ketamine administered with propofol to evoke deep sedation levels during painful ED procedures.[11-20]

General anesthesia: General anesthesia describes a depth of sedation characterized by unresponsiveness to all stimuli and the absence of airway protective reflexes, a pharmacologically induced loss of consciousness during which patients are not arousable, even by painful stimulation. The ability to independently maintain ventilatory function is often impaired. Patients often require assistance in maintaining a patent airway, and positive-
pressure ventilation may be required because of depressed spontaneous ventilation or drug-induced depression of neuromuscular function. Cardiovascular function may be impaired.[1,5,10]

METHODOLOGY

This clinical policy was created after careful review and critical analysis of the medical literature. Searches of MEDLINE, MEDLINE InProcess, Cochrane Systematic Review Database, and Cochrane Database of Clinical Trials were performed. All searches were limited to English-language sources, human studies, pediatrics, and adults. Specific key words/phrases and years used in the searches are identified under each critical question. In addition, relevant articles from the bibliographies of included studies and more recent articles identified by committee members and reviewers were included.

This policy is a product of the ACEP clinical policy development process, including expert review, and is based on the existing literature; when literature was not available, consensus of emergency physicians was used. Expert review comments were received from emergency physicians, pediatric emergency medicine physicians, toxicologists, a pediatric anesthesiologist, a pharmacist, and individual members of the American Academy of Pediatrics, the American College of Medical Toxicology, ACEP's Emergency Medicine Practice Committee, Medical-Legal Committee, and Pediatric Emergency Medicine Committee, ACEP's Toxicology Section, and ACEP's Emergency Medicine Workforce Section. The draft was also open to comments from ACEP membership through *EM Today*. Their responses were used to further refine and enhance this policy; however, their responses do not imply endorsement of this clinical policy. Clinical policies are scheduled for revision every 3 years; however, interim reviews are conducted when technology or the practice environment changes significantly. The ACEP was the funding source for this clinical policy.

Assessment of Classes of Evidence

All articles used in the formulation of this clinical policy were graded by at least 2 subcommittee members and assigned a Class of Evidence. In doing so, subcommittee members assigned design classes to each article, with design 1 representing the strongest study design and subsequent design classes (eg, design 2, design 3) representing respectively weaker study designs for therapeutic, diagnostic, or prognostic clinical reports, or meta-analyses (Appendix A). Articles were then graded on dimensions related to the study's methodological features, including but not necessarily limited to randomization processes, blinding, allocation concealment, methods of data collection, outcome measures and their assessment, selection and misclassification biases, sample size, and generalizability. Using predetermined formulas related to the study's design, methodological quality, and applicability to the critical question, articles received a final Class of Evidence grade (ie, Class I, Class II, Class III, or Class X) (Appendix B). Articles identified with fatal flaws or that were not applicable to the critical question received a Class of Evidence grade "X" and were not used in formulating recommendations for this policy. Grading was done with respect to the specific critical questions; thus, the level of evidence for any one study may vary according to the question. As such, it was possible for a single article to receive different Classes

of Evidence as different critical questions were answered from the same study. Question-specific Classes of Evidence grading may be found in the Evidentiary Table included at the end of this policy.

Translation of Classes of Evidence to Recommendation Levels

Strength of recommendations regarding each critical question were made by subcommittee members using results from strength of evidence grading, expert opinion, and consensus among subcommittee members according to the following guidelines:

Level A recommendations. Generally accepted principles for patient care that reflect a high degree of clinical certainty (ie, based on evidence from 1 or more Class of Evidence I or multiple Class of Evidence II studies).

Level B recommendations. Recommendations for patient care that may identify a particular strategy or range of strategies that reflect moderate clinical certainty (ie, based on evidence from 1 or more Class of Evidence II studies or strong consensus of Class of Evidence III studies).

Level C recommendations. Recommendations for patient care that are based on evidence from Class of Evidence III studies or, in the absence of any adequate published literature, based on expert consensus. In instances in which consensus recommendations are made, "consensus" is placed in parentheses at the end of the recommendation.

There are certain circumstances in which the recommendations stemming from a body of evidence should not be rated as highly as the individual studies on which they are based. Factors such as heterogeneity of results, uncertainty about effect magnitude and consequences, and publication bias, among others, might lead to such a downgrading of recommendations.

When possible, clinically oriented statistics (eg, likelihood ratios, number needed to treat) were presented to help the reader better understand how the results may be applied to the individual patient. For a definition of these statistical concepts, see Appendix C.

This policy is not intended to be a complete manual on the evaluation and management of patients undergoing procedural sedation and analgesia but rather a focused examination of critical issues that have particular relevance to the current practice of emergency medicine.

It is the goal of the Clinical Policies Committee to provide an evidence-based recommendation when the medical literature provides enough quality information to answer a critical question. When the medical literature does not contain adequate empirical data to answer a critical question, the members of the Clinical Policies Committee believe that it is equally important to alert emergency physicians to this fact.

Recommendations offered in this policy are not intended to represent the only diagnostic or management options available to the emergency physician. ACEP clearly recognizes the importance of the individual physician's judgment and patient preferences. Rather, this guideline defines for the physician those strategies for which medical literature exists to provide support for answers to the critical questions addressed in this policy.

Scope of Application. This guideline is intended for physicians working in EDs.

Inclusion Criteria. This guideline is intended for patients of all ages in the ED who have emergent or urgent conditions that require pain and/or anxiety management to successfully accomplish an interventional or diagnostic procedure and for high-risk patients (eg, those with underlying cardiopulmonary disorders, multiple trauma, head trauma, who have ingested a central nervous system depressant such as alcohol), with the understanding that these patients are at increased risk of complications from procedural sedation and analgesia.

Exclusion Criteria. This guideline is not intended for patients receiving inhalational anesthetics, patients who receive analgesia for pain control without sedatives, patients who receive sedation solely for the purpose of managing anxiolysis and behavioral emergencies, and patients who are intubated.

CRITICAL QUESTIONS

1. In patients undergoing procedural sedation and analgesia in the emergency department, does preprocedural fasting demonstrate a reduction in the risk of emesis or aspiration?

Recommendations

Level A recommendations. None specified.

Level B recommendations. Do not delay procedural sedation in adults or pediatrics in the ED based on fasting time. Preprocedural fasting for any duration has not demonstrated a reduction in the risk of emesis or aspiration when administering procedural sedation and analgesia.

Level C recommendations. None specified.

Key words/phrases for literature searches: conscious sedation, sedation, procedural sedation, procedural analgesia, moderate sedation, deep sedation, fasting, gastric emptying, complication, aspiration, emesis, and variations and combinations of the key words/phrases; years January 2004 to May 2012.

Emesis or aspiration during procedural sedation in the ED is rare.[21] For healthy patients undergoing elective sedation/analgesia, other professional society guidelines outside of emergency medicine recommend a 2-hour fasting time for clear liquids, 4-hour fasting time for breast milk, and a 6-hour fasting time for solids. However, the guidelines are based on the extrapolation of general anesthesia cases in the operating room, in which airway manipulation during intubation and extubation increases the aspiration risk. Thus, it is not clear whether applying these guidelines to ED procedural sedation and analgesia reduces the risk of emesis or aspiration. Moreover, even within the framework of these guidelines, emergent sedations are an exclusion from fasting requirements.[22]

As a result, guidelines for elective procedures in the operating room (eg, nothing by mouth, preoperative fasting guidelines) are not directly applicable in the ED. In addition, multiple other practice guidelines and systematic reviews do not find evidence to support a specific fasting period before ED procedural sedation. Two systematic reviews[23,24] and 2 practice advisories[11,25] acknowledge the lack of evidence to support specific preprocedural fasting requirements.

Four Class II trials with pediatric patients[26-29] and 1 Class II trial with adult and pediatric patients[30] examined the effect of fasting time (0 to >8 hours) on emesis and aspiration during ED procedural sedation. None of these studies demonstrated a significant difference in rates of emesis or aspiration when comparing fasting times. In addition, no serious adverse events caused by emesis or aspiration were found. The current evidence does not support the rationale put forth in the non–emergency medicine guidelines that adhering to a minimum fasting time reduces adverse events in ED procedural sedation.

Roback et al[26] performed a single-center study of 1,555 pediatric patients undergoing procedural sedation with ketamine, midazolam, midazolam/ketamine, midazolam/fentanyl, and a small number of other agents. The study found no relationship between fasting time and the proportion of patients with adverse events. Respiratory adverse events were defined as apnea, laryngospasm, pulse oximetry less than 90% on room air at the elevation of the study site (5,280 feet), and aspiration. Any adverse events (vomiting or adverse respiratory event) occurred in

12.0% in the 0- to 2-hour group, 16.4% in the 2- to 4-hour group, 14.0% in the 4- to 6-hour group, 14.6% in the 6- to 8-hour group, and 14.5% in the greater than 8 hours group. Using the group that fasted 0 to 2 hours as the reference group, the difference in proportion of any adverse events was 4.3% in the 2- to 4-hour group, 2.0% in the 4- to 6-hour group, 2.6% in the 6- to 8-hour group, and 2.5% in the greater than 8 hours group. There were no aspiration events documented in the entire cohort of 1,555 patients.

Treston[27] included 257 pediatric patients undergoing procedural sedation with ketamine. In this study also, fasting time did not correlate with the incidence of emesis, which occurred in 6.6% in the 1 hour or less fasting group, 14.0% in the 1- to 2-hour fasting group, and 15.7% in the 3 hours or greater group. Using the group that fasted 1 hour or less as the reference group, the difference in proportion of vomiting in the 1- to 2-hour fasting group was 7.3%; in the 3-hour or greater group, 9.1%. No clinically detectable aspiration occurred, and no airway maneuvers or suctioning was required.

Babl et al[28]conducted a study of 218 consecutive pediatric patients undergoing procedural sedation with nitrous oxide. Fasting guidelines for solids were not met by 71.1% of the patients. There was no statistical difference in incidence of emesis, which occurred in 7.1% of patients who did not meet fasting guidelines for solids compared with 6.3% in those who met guidelines. Serious adverse events were defined as pulse oximetry less than 95%, apnea, stridor, airway misalignment requiring repositioning, laryngospasm, bronchospasm, cardiovascular instability, pulmonary aspiration, unplanned hospital admission, endotracheal intubation, permanent neurologic injury, or death. There were no serious adverse events observed.

McKee et al[29] examined 471 pediatric patients undergoing procedural sedation with ketamine, in which presedation oral analgesic administration was recorded. In this Class II study, 42.7% of patients received oral analgesics within 6 hours of sedation. Emesis occurred in 5.0% of patients who received oral analgesics compared with 2.6% of patients who did not receive oral analgesics. Additional adverse events recorded were hypoxia (desaturation requiring supplemental oxygen), hypoventilation, laryngospasm, apnea, bradycardia, or tachycardia. Total adverse events were similar for patients receiving oral analgesia (5.0%) and those not receiving oral analgesia (5.6%). The authors did not report episodes of intubation, aspiration, unplanned admission, or death, although these were not explicit outcome measures in the study.

Bell et al[30] followed 400 adult and pediatric patients undergoing procedural sedation with propofol. The authors found that 70.5% of those enrolled did not meet American Society of Anesthesiologists (ASA) fasting guidelines for solids or liquids. They identified no significant difference between the groups meeting and not meeting fasting guidelines with respect to adverse events that included emesis and respiratory interventions. Emesis occurred in 0.4% of patients who did not meet fasting guidelines compared with 0.8% of those who met guidelines. The combined endpoint of respiratory adverse events was defined as transient apnea, pulse oximetry less than 95%, respiratory rate less than 12 breaths/min, elevated end-tidal carbon dioxide ($ETCO_2$) greater than 10 mm Hg, vomiting, and aspiration. Respiratory adverse events occurred in 22.4% of patients who did not meet fasting guidelines compared with 19.5% of those who met guidelines. With only 2 episodes of emesis and no aspiration events, this combined endpoint was driven primarily by interventions less likely to be related to fasting, such as respiratory depression and desaturation. The combined endpoint of respiratory interventions was defined as basic airway maneuvers, Guedel/bag-valve-mask, and suctioning. Respiratory interventions occurred in 33.3% of patients who did not meet fasting guidelines compared with 24.6% of those who met guidelines. With only 3 interventions requiring suctioning, this combined endpoint is predominantly weighted by basic airway and bag-valve-mask interventions, which are less likely to be affected by fasting. There were no aspiration events, intubations, laryngeal mask airway insertions, or unplanned admissions related to sedation or recovery in either group.

Future research should focus on the identification of a potential high-risk population that might benefit from a fasting time or a sedation agent with better efficacy after patient fasting if such a delay is to be relevant in any ED procedural sedations. In addition, research into the harms of enforcing fasting periods would bring balance to the literature. Concerns about procedural difficulty, ED resource utilization, and pediatric hypoglycemia related to enforced fasting periods for ED procedural sedation have not been evaluated.

2. In patients undergoing procedural sedation and analgesia in the emergency department, does the routine use of capnography reduce the incidence of adverse respiratory events?

Recommendations

Level A recommendations. None specified.

Level B recommendations. Capnography* may be used as an adjunct to pulse oximetry and clinical assessment to detect hypoventilation and apnea earlier than pulse oximetry and/or clinical assessment alone in patients undergoing procedural sedation and analgesia in the ED.

*Capnography includes all forms of quantitative exhaled carbon dioxide analysis.

Level C recommendations. None specified.

Key words/phrases for literature searches: sedation, procedural sedation and analgesia, conscious sedation, moderate sedation, deep sedation, capnography, end tidal carbon dioxide, complications, adverse events, and variations and combinations of the key words/phrases; years January 2004 to May 2012.

Capnography allows continuous measurement of exhaled carbon dioxide and displays the resulting waveform graphically. It provides an advantage over pulse oximetry alone by identifying respiratory depression more consistently. Capnometry is the numeric display of exhaled carbon dioxide concentrations. $ETCO_2$ is the highest value of carbon dioxide measured during the end of expiration of each breath. These measurements can be used to assess the adequacy of ventilation during procedural sedation and analgesia. Detectable respiratory events such as hypoxia, respiratory depression, and/or apnea are common and may be precursors of more serious events during procedural sedation and analgesia.[31-33] Monitoring of $ETCO_2$ detects hypoventilation earlier than methods such as pulse oximetry and pulse rate alone, particularly when supplemental oxygen is administered.[34-38] However, adverse respiratory events leading to serious patient-centered outcomes, such as aspiration, unplanned intubation, or cardiac arrest, are exceedingly rare events in procedural sedation and analgesia both within and outside of the ED.[39,40] In an attempt to minimize these adverse events further, the routine use of capnography monitoring during all procedural sedation and analgesia has been recommended.[7,41] Both the diagnostic monitoring performance and clinical benefit of capnography have been studied.[31-36]

Waugh et al[34] published a Class III meta-analysis of capnography as a monitoring device. This systematic review included 5 studies, 3 Class III studies performed in the ED,[35-37] one Class III study performed outside of the ED,[38] and a study graded an X for this question.[42] This meta-analysis reported improved diagnostic performance with capnography. In the meta-analysis, capnography was 17.6 (95% confidence interval [CI] 2.5 to 122) times more likely to detect respiratory depression than standard monitoring alone. This meta-analysis is limited by the range of definitions across studies of hypoxia and respiratory depression, capnography results used in the definition of respiratory depression leading to incorporation bias, individual single-center studies of limited

power, and results showing significant heterogeneity. Results of each of the included studies in the meta-analysis were graded and are discussed below.

The first ED trial, a Class III study in 2002 by Miner et al,[35] demonstrated that all episodes of respiratory depression were detected by carbon dioxide monitoring, whereas pulse oximetry detected only 33%. There was no correlation between capnography and provider observation as measured by the Observer Assessment of Alertness/Sedation Scale.

The second Class III ED study was performed by Burton et al[36] in 2006. In this study of 60 patients, 60% had abnormal $ETCO_2$ levels, and 56% of these went on to have respiratory events defined broadly as ranging from oxygen desaturation below 92%, to any intervention, including supplemental oxygen, directed verbal stimuli, repositioning, and/or bag-mask-valve ventilation as a result of hypoventilation or apnea. $ETCO_2$ abnormalities were demonstrated before pulse oximetry in 70% of the patients with these events. Similar results were reported by Vargo et al[38] during procedural sedation and analgesia for upper endoscopy, with 100% of respiratory events detected by capnography, 50% by pulse oximetry, and none by provider observation.

Last, in a Class III study by Deitch et al,[37] propofol with supplemental oxygen versus room air in procedural sedation was compared. This study also assessed the ability to detect respiratory depression by the provider compared with the addition of capnography. Physicians were able to detect respiratory depression in 92% of the patients who developed hypoxia but in only 3.7% of the patients with respiratory depression who did not develop hypoxia.

Deitch et al[43,44] also performed 2 similar Class III studies with other agents and variable amounts of oxygen supplementation. In a 2007 study of 80 patients with supplemental oxygen versus room air during sedation with fentanyl and midazolam, 35% of patients had respiratory depression, with none of these episodes detected by the providers.[43] In a 2011 study of 117 patients with high-flow oxygen versus room air during sedation with midazolam and fentanyl, 49% of patients had respiratory depression, but this was detected only in 25% of patients by pulse oximetry.[44] Finally, Anderson et al[45] performed another Class III study with propofol sedation in pediatric orthopedic procedures, in which 100% of the episodes of apnea and 60% of the episodes of airway obstruction were detected by capnography before pulse oximetry.

Whether use of capnography provides clinically important benefit has been evaluated in a variety of settings. Evidence from 2 studies performed outside the ED has demonstrated decreased hypoxia with the use of capnography. Lightdale et al[31] performed a Class II randomized trial of capnography use during pediatric endoscopy and showed a significant reduction in hypoxia, from 24% to 11%. In a similar Class II study performed in adult endoscopy, Qadeer et al[32] reported a reduction in hypoxia from 69% to 46% with the use of capnography. In 2010, Deitch et al[33] performed a Class II randomized, controlled trial to determine whether capnography decreases the incidence of hypoxic events in patients receiving propofol for procedural sedation and analgesia in the ED. This study reported a sensitivity of 100% (95% CI 90% to 100%) and specificity of 64% (95% CI 53% to 73%). More important, it demonstrated a benefit with an absolute risk reduction of 17% (95% CI 1.3% to 33%) related to hypoxia. One Class III study performed by Sivilotti et al[46] did not detect a statistically significant benefit (odds ratio 1.4 [95% CI 0.47 to 4.3]), but this study was not primarily designed to address the use of capnography.

Although the routine use of capnography appears to decrease the incidence of hypoxia and respiratory events as defined in these studies (Level B recommendation), currently there is a lack of evidence that capnography reduces the incidence of serious adverse events during procedural sedation and analgesia such as neurologic injury caused by hypoxia, aspiration, or death. Future studies should focus on these areas to provide a better understanding of these outcomes.

3. In patients undergoing procedural sedation and analgesia in the emergency department, what is the minimum number of personnel necessary to manage complications?

Recommendations

Level A recommendations. None specified.

Level B recommendations. None specified.

Level C recommendations. During procedural sedation and analgesia, a nurse or other qualified individual should be present for continuous monitoring of the patient, in addition to the provider performing the procedure. Physicians who are working or consulting in the ED should coordinate procedures requiring procedural sedation and analgesia with the ED staff.

Key words/phrases for literature searches: conscious sedation, sedation, procedural sedation, moderate sedation, deep sedation, personnel, complications, adverse events, and variations and combinations of the key words/phrases; years January 2004 to May 2012.

Procedural sedation and analgesia, including moderate and deep levels, has been demonstrated to be both safe and effective when properly administered by experienced emergency physicians.[47-56] Personnel providing procedural sedation and analgesia must have an understanding of the medications used, the ability to monitor the patient's response to those medications, and the skills necessary to intervene in managing potential complications. The determination of specific medications for procedural sedation that may be safely administered by a nurse with provider supervision is beyond the scope of this critical question. However, in a 2011 statement, ACEP expressed strong support for qualified ED nurses to administer propofol, ketamine, and other sedatives under the direct supervision of a privileged emergency physician.[57] Individuals considered qualified to monitor patients for complications should be capable of detecting events such as hypotension, hypoventilation, hypoxia, and dysrhythmias.

Sedation to anesthesia is a continuum, and it is not always possible to predict how individual patients receiving medications will respond. The Joint Commission stipulates that "individuals administering moderate or deep sedation and anesthesia are qualified and have credentials to manage and rescue patients at whatever level of sedation or anesthesia is achieved, either intentionally or unintentionally."[6] It is important for institutions to ensure that all individuals permitted to supervise moderate or deep sedation are able to (1) choose appropriate pharmacologic agents; (2) monitor patients to detect complications such as hypotension, hypoventilation, hypoxia, and dysrhythmias; and (3) manage the potential complications.

The literature does not provide clear evidence on the number and type of personnel necessary to safely provide procedural sedation and analgesia. There are 2 Class III studies reporting data from the same observational database comprised of more than 1,000 consecutive emergency-directed procedural sedation cases.[58,59] The rate of complications defined as airway obstruction, apnea, hypotension, and hypoxia was similar (ie, approximately 4%) whether a single physician administered the sedation and performed the procedure or 2 physicians were present, with 1 administering the sedation and the other performing the procedure. In both scenarios, a nurse was present to monitor the patient. All complications were resolved successfully and no patient

experiencing a complication required hospital admission.[58,59] These Class III studies were primarily limited by the fact that the decision to staff 1 or 2 physicians was not randomized or determined a priori. The physicians were allowed to choose which staffing they believed was appropriate on a case-by-case basis and then the 2 personnel models were compared. Similarly, in a third Class III study that specifically looked at 457 sedations in ED patients with orthopedic injuries requiring procedural sedation and analgesia, there was no difference in the incidence of adverse events requiring intervention between cases using a 1 physician and 1 nurse model compared with a 2 physician and 1 nurse model. Adverse events requiring intervention in this study were defined as those events requiring one or more of the following: vigorous tactile stimulation, airway repositioning (chin lift, jaw thrust, neck extension, midline repositioning), suctioning, supplemental or increased oxygen delivery, placement of oral or nasal airway, application of positive pressure or ventilation with bag mask, tracheal intubation (laryngeal mask airway or endotracheal tube intubation), administration of reversal agents (flumazenil or naloxone), administration of antidysrhythmic agents, and chest compressions. All adverse events requiring intervention in this study were resolved successfully and none resulted in subsequent sequelae.[60]

Although it would seem reasonable that some patients with more complex needs may require 2 physicians for the safe practice of procedural sedation and analgesia in the ED, there is no evidence that specifically identifies which cases, if any, require dual-physician involvement to prevent adverse outcome. ED providers supervising procedural sedation and analgesia appear capable of determining whether additional resources are necessary to complete the procedure safely.

Future studies of the staffing necessary for procedural sedation and analgesia should measure patient-centered outcomes, as well as control for the type of medication and dosing administered, type of procedure performed, type of medical personnel present, patient comorbidities, and current clinical condition.

4. In patients undergoing procedural sedation and analgesia in the emergency department, can ketamine, propofol, etomidate, dexmedetomidine, alfentanil, and remifentanil be safely administered?

Recommendations

Level A recommendations. Ketamine can be safely administered to children for procedural sedation and analgesia in the ED. Propofol can be safely administered to children and adults for procedural sedation and analgesia in the ED.

Level B recommendations. Etomidate can be safely administered to adults for procedural sedation and analgesia in the ED. A combination of propofol and ketamine can be safely administered to children and adults for procedural sedation and analgesia.

Level C recommendations. Ketamine can be safely administered to adults for procedural sedation and analgesia in the ED. Alfentanil can be safely administered to adults for procedural sedation and analgesia in the ED. Etomidate can be safely administered to children for procedural sedation and analgesia in the ED.

Key words/phrases for literature searches: ketamine, propofol, etomidate, dexmedetomidine, remifentanil, fentanyl, adverse events, procedural sedation, conscious sedation, deep sedation, and variations and combinations of the key words/phrases; years January 2004 to May 2012.

During recent years, there has been a continuously growing body of evidence addressing ketamine, midazolam, fentanyl, propofol, and etomidate that significantly adds to the depth of understanding of these agents' use in the ED.[1,11-20,30,39,43,58,61-88]

The use of short-acting sedative agents such as propofol and etomidate for ED procedural sedation and analgesia has gained widespread acceptance. Brief-acting sedative agents confer shorter periods of impaired levels of consciousness and subsequently less risk for adverse respiratory events.[62,71-73,75] An additional benefit to shorter periods of patient impaired consciousness is a reduction of patient monitoring time that allows reduced allocations of intense patient monitoring periods by medical and nursing staff.

Propofol is an agent that has attracted a great deal of attention by investigators and publications since the previous clinical policy was published.[1] Since then, multiple studies have demonstrated findings that support and strengthen the use of propofol for both adult and pediatric patients.[15,17,18,30,39,43,62-69,83,88] These investigations include a Class I study,[15] 2 Class II studies,[66,83] and multiple Class III investigations.[30,64,65] The patient population across studies reporting use of propofol as a procedural sedation and analgesia agent in the ED setting is currently well in excess of 26,000.[39,62,63]

The combination of ketamine and propofol ("ketofol") has gained a degree of interest for ED procedural sedation and analgesia patients.[12-20,69] These investigations and reports include 1 Class I study in pediatric patients,[16] a Class I study with both pediatric and adult patients,[15] and a single Class III study in adults.[14] This intravenous combination typically allows drug dosing that is less than that used with either propofol or ketamine as a sole agent. Studies using ketamine or propofol as a single agent in ED procedural sedation and analgesia

routinely use 1.0 mg/kg as an initial dosing regimen for each drug. When ketamine and propofol are combined during ED procedural sedation and analgesia, dosing regimens typically use approximately 0.5 mg/kg to 0.75 mg/kg for each agent. An additional advantage of this combination strategy has been argued to be a reduction in the adverse risks associated with propofol and ketamine.[12-16,20,69] Propofol-associated hypotension and respiratory depression can theoretically be reduced with increases in circulatory norepinephrine induced by ketamine. Similarly, the relatively greater risks for ketamine-associated nausea and emergence reactions are theoretically reduced by the antiemetic and anxiolytic properties of propofol. Studies have demonstrated a reduction in concomitant analgesic agent when a ketamine and propofol combination is used simultaneously in comparison to administration of propofol as a single agent.[17,18]

In the 2 Class I studies, the combination of ketamine and propofol, when compared with a single-drug procedural sedation and analgesia regimen of either ketamine or propofol, resulted in higher provider satisfaction with the sedation encounter.[15,16] In both of these studies, respiratory depression rates were similar between the treatment groups. In the Class I study involving a pediatric population, the total patient sedation times were shorter, an approximate 19% reduction of 3 minutes, with the combined ketamine and propofol regimen compared with ketamine alone in pediatric procedural sedation and analgesia patients.[16]

Ketamine is widely used for children undergoing procedural sedation and analgesia in the ED. Multiple studies have continued to support this practice.[11,70-76,89] Studies addressing the use of ketamine as a sole agent in the adult procedural sedation and analgesia ED population have also been published.[77,78] Intravenous ketamine use in the adult population remains less common, likely because of reported rates of emergence phenomena, including recovery agitation.[79]

Studies have continued to address the administration of adjunctive agents with ketamine separate from propofol.[80-82] In a double-blind, randomized, placebo-controlled trial, Langston et al[80] demonstrated a significant reduction in vomiting with the use of ondansetron in pediatric patients receiving ketamine for ED procedural sedation and analgesia. No adverse events were associated with the use of ondansetron in this trial. Two trials reported an assessment of atropine as an additional agent during ketamine ED procedural sedation and analgesia.

Brown et al[81] reported a reduction in observed hypersalivation, although hypersalivation associated with ketamine use during ED procedural sedation and analgesia appears to uncommonly have clinical implications.[81,82]

Recent studies have evaluated the use and safety of etomidate in both adult and pediatric patients, including studies comparing it with other ED procedural sedation and analgesia agents.[58,83-85] Etomidate has clinical characteristics similar to those of propofol including onset of sedation, sedation depth, and duration of clinical effects. One disadvantage of etomidate use during procedural sedation is etomidate-associated myoclonus.[83] Myoclonus has been described extensively with clinical events that range from mild to severe in 20% to 40% of patients receiving etomidate during ED procedural sedation and analgesia.[90,91] These myoclonus events uncommonly result in clinically significant effects. Although trials investigating etomidate-induced adrenal suppression in procedural sedation are not available, numerous studies have demonstrated cortisol depression for up to 24 hours with as little as a single dose of etomidate. However, the levels consistently remain in the normal range, with no clinically significant sequelae.[92-95]

Reports and studies addressing new sedative agents in ED procedural sedation and analgesia have been few since the previous clinical policy.[1] Alfentanil is an agent that has been described for procedural sedation and analgesia in the ED.[66,87] Alfentanil is an ultrashort-acting analogue of fentanyl. Miner et al,[66] in a Class II study, reported alfentanil to be safe and effective when added to propofol procedural sedation and analgesia in the ED. They noted an increase in patients who required stimulation to induce ventilation during ED procedural sedation and analgesia among the supplemental alfentanil patients. The authors subsequently concluded there was no benefit derived from the addition of alfentanil to propofol with regard to rates of hypoventilation. In this study, recovery rates were noted to be longer when alfentanil was added to propofol as part of the propofol procedural sedation and analgesia regimen.[66]

Remifentanil is an ultrashort-acting synthetic opioid used in general anesthesia for sedation and analgesia, and has been described in brief reports for ED procedural sedation and analgesia.[88,96] Dexmedetomidine is a newer sedative agent. To date, only a case report has been published addressing the use of dexmedetomidine in the ED procedural sedation and analgesia population.[97]

Future studies should seek to contribute to the body of evidence about the safety and efficacy profile of the multiple classes of sedative agents used for ED procedural sedation and analgesia. As newer agents that are similar in function to existing drugs become available, future policies should focus on the safety and efficacy of sedative agents according to their classification rather than the specific agent alone.

CONCLUSION

Safe and effective sedation and analgesia in the ED is a critical skill that is core to the practice of emergency medicine. Successful performance requires recognition of not only pitfalls associated with the medications but also consideration for the complexity of patients' underlying physiology and illness or injury. Emergency physicians are qualified to manage sedation requirements across all ages, involving a broad range of complicated patient presentations. It is clear that in typical ED populations, sedation is both safe and effective in providing increased patient comfort and ease of procedural performance.

Future ED studies should further investigate the unique sedation challenges encountered in high-risk patient subgroups to identify best practices for procedural sedation monitoring and performance. Further, the potential effect of various environments of care encountered across different EDs should also be considered when evaluating the safe performance of procedural sedation. Ultimately, a focus on patient-centered outcomes should be the prevailing core principle by which these future studies are designed.

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883 **Evidentiary Table.**

Study	Year	Design	Intervention(s)/Test(s)/ Modality	Outcome Measure/Criterion Standard	Results	Limitations/ Comments	Class
Andolfatto and Willman[14]	2011	Prospective, uncontrolled, observational trial	Adult patients 21 y of age or older receiving ketofol as a 1:1 mixture of 10 mg/mL propofol and 10 mg/mL ketamine	Patients evaluated for drug dosages administered, adverse events, recovery time; patient and staff satisfaction were recorded	728 patients received a median ketofol dose of 0.7 mg/kg with median recovery time of 14 min; ketofol administered primarily for orthopedic procedure patients; complications included BVM use in 2.1%, apnea in 0.5%, and hypoxia in 0.3%; recovery agitation was reported in 3.6%, with 1.8% of all study patients requiring treatment for recovery agitation; rigidity was reported in 1.5% of patients; excess secretions noted in 1 patient with vomiting in 1 patient; dysrhythmia and hypotension were reported in 1 patient who required admission; staff and patients reported satisfaction as high	Design limitations included nonblinded, nonrandomized enrollment, with no comparative group; premedication not standardized; enrollment of patients limited by physician selection bias and convenience	III

884

885 **Evidentiary Table (continued).**

Study	Year	Design	Intervention(s)/Test(s)/ Modality	Outcome Measure/Criterion Standard	Results	Limitations/ Comments	Class
David and Shipp[15]	2011	Double blinded, randomized, placebo-controlled trial	Adult and pediatric patients treated with IV fentanyl by protocol and then randomized to treatment protocol with either placebo or ketamine administered as a bolus of 0.5 mg/kg; both treatment groups then received IV propofol by protocol dosing with 1.0 mg/kg bolus followed by 0.5 mg/kg bolus doses as needed	Primary outcome variable was the rate of predefined, observed respiratory depression; secondary outcomes included dose of propofol, provider satisfaction, and sedation quality	200 subjects enrolled with 110 randomized to receive placebo and 110 to the ketamine treatment arm; 96 placebo and 97 ketamine patients completed the study; sedation performed primarily for orthopedic and suturing procedures; baseline characteristics were similar between groups except for more male patients in the placebo group; respiratory depression was similar between the groups, with 22% of ketamine patients experiencing respiratory depression compared with 28% of placebo patients; provider satisfaction with sedation was higher in the ketamine group; patients in the ketamine group received less propofol	Blinding limited in the study because of nystagmus and secretions in ketamine group; nystagmus blinded by use of sunglasses; no secretions reported in any patients	I

886

887 **Evidentiary Table (continued).**

Study	Year	Design	Intervention(s)/Test(s)/ Modality	Outcome Measure/Criterion Standard	Results	Limitations/ Comments	Class
Shah et al[16]	2011	Double-blinded, randomized, controlled study	Pediatric orthopedic ED patients randomized to treatment protocol with either ketamine 1.0 mg/kg as initial bolus plus ketamine 0.25 mg/kg as needed or propofol/ketamine administered as 0.5 mg/kg propofol plus 0.5 mg/kg ketamine initial bolus with additional ketamine 0.25 mg/kg as needed	Primary outcome variable was the total sedation time; secondary outcomes included time to recovery, efficacy, adverse events, and provider satisfaction	136 subjects enrolled with 69 randomized to receive ketamine alone and 67 to the propofol/ketamine treatment arm; baseline characteristics were similar between groups; total sedation time and recovery time were shorter with propofol/ketamine; there was less vomiting and higher satisfaction with propofol/ketamine; respiratory depression was similar between the groups	Opiate and O_2 treatment not standardized in the treatment protocol	I

888

Evidentiary Table (continued).

Study	Year	Design	Intervention(s)/Test(s)/ Modality	Outcome Measure/Criterion Standard	Results	Limitations/ Comments	Class
Roback et al[26]	2004	Prospective observational cohort study	Single-center study of 1,555 pediatric patients undergoing procedural sedation	Case definition: patient fasting times of 0-2 h (reference group), 2-4 h, 4-6 h, 6-8 h, and >8 h; outcomes: emesis and adverse respiratory events (apnea, laryngospasm, desaturations, and aspiration)	Adverse events (vomiting or adverse respiratory event) occurred in 18/150 (12%) in the 0- to 2-h group, 64/391 (16.4%) in the 2- to 4-h group, 60/430 (14%) in the 4- to 6-h group, 41/281 (14.6%) in the 6- to 8-h group, and 44/303 (14.5%) in the >8-h group; using the group that fasted 0-2 h as the reference group, the difference in proportion of any adverse events was 4.3% (95% CI -2.0% to 10.7%) in the 2- to 4-h group, 2.0% (95% CI -4.2% to 8.1%) in the 4- to 6-h group, 2.6% (95% CI -4.0% to 9.2%) in the 6-to 8-h group, and 2.5% (95% CI -4.0 to 9.1%) in the >8-h group;* compared with the group that fasted for 0-2 h, the OR for adverse events in the 2- to 4-h group was 1.4 (95% CI 0.8 to 2.5), in the 4-to 6-h group 1.2 (95% CI 0.7 to 2.1), in the 6- to 8-h group 1.3 (95% CI 0.7 to 2.3), and in the >8-h group 1.3 (95% CI 0.7 to 2.2); there were no aspiration events documented in the entire cohort of 1,555 patients (0%; 95% CI 0% to 0.2%)*	One fourth of patients in the initial cohort were excluded; the adverse event rate in this group was not different from that in the groups in which fasting status was documented; distinction between solids and liquid fasting time was not consistently documented; did not evaluate rationale for some patients meeting fasting guidelines and others not meeting guidelines; outcome measured with knowledge of fasting status; multiple sedation agents used	II

*Calculations of 95% CI and difference in proportions were performed in Stata version11.2 when not reported in the original article.

Evidentiary Table (continued).

Study	Year	Design	Intervention(s)/Test(s)/ Modality	Outcome Measure/Criterion Standard	Results	Limitations/ Comments	Class
Treston[27]	2004	Prospective observational cohort study	Single-center study of 257 pediatric patients undergoing procedural sedation with ketamine	Case definition: patient fasting times of 1 h, 2-3 h, and >3 h; outcome: emesis	Vomiting occurred in 2/30 (6.6%) in the 1 h or less fasting group, 14/100 (14.0%) in the 1- to 2-h fasting group, and 20/127 (15.7%) in the 3 h or greater group; using the group that fasted 1 h or less as the reference group, the difference in proportion of vomiting in the 1- to 2-h fasting group was 7.3% (95% CI -3.9% to 18.5%) and in the 3-h or greater group was 9.1% (95% CI -1.9% to 20.0%);* no clinically detectable aspiration occurred and no airway maneuvers or suctioning was required (0%; 95% CI 0% to 1.4%).*	Not powered to detect a difference in emesis rate; did not evaluate rationale for some patients meeting fasting guidelines and others not meeting guidelines; outcome measured with knowledge of fasting status	II

*Calculations of 95% CI and difference in proportions were performed in Stata version11.2 when not reported in the original article.

Evidentiary Table (continued).

Study	Year	Design	Intervention(s)/Test(s)/ Modality	Outcome Measure/Criterion Standard	Results	Limitations/ Comments	Class
Babl et al[28]	2005	Prospective observational cohort study	Single-center study of 218 consecutive pediatric patients undergoing procedural sedation with nitrous oxide	Case definition: patients not meeting ASA fasting guideline (6 h for solids and 2 h for liquids); outcome: emesis	155/218 (71.1%) did not meet fasting guidelines for solids; emesis occurred in 11/155 (7.1%) of those who did not meet fasting guidelines for solids compared with 4/63 (6.3%) in those who met guidelines (difference=0.7%; 95% CI -6.5% to 8.0%);* serious adverse events were defined as desaturation less than 95% SpO_2, apnea, stridor, airway misalignment requiring repositioning, laryngospasm, bronchospasm, cardiovascular instability, pulmonary aspiration, unplanned hospital admission, endotracheal intubation, permanent neurologic injury, or death; there were no serious adverse events observed (0%; 95% CI 0% to 1.7%)	Not powered to detect a difference in emesis rate; convenience sample; did not evaluate rationale for some patients meeting fasting guidelines and others not meeting guidelines; outcome measured with knowledge of fasting status	II

*Calculations of 95% CI and difference in proportions were performed in Stata version11.2 when not reported in the original article.

898 **Evidentiary Table (continued).**

Study	Year	Design	Intervention(s)/Test(s)/ Modality	Outcome Measure/Criterion Standard	Results	Limitations/ Comments	Class
McKee et al[29]	2008	Prospective observational cohort study	Single-center study of 471 pediatric patients undergoing procedural sedation with ketamine	Case definition: patients receiving oral analgesic before sedation; outcome: emesis	201/471 (42.7%) received oral analgesics within 6 h of sedation; emesis occurred in 10/201 (5.0%) patients who received oral analgesics compared with 7/270 (2.6%) patients who did not receive oral analgesics, difference=2.4% (95% CI -1.1% to 6.5%); additional adverse events recorded were hypoxia (desaturation requiring supplemental O_2), hypoventilation, laryngospasm, apnea, bradycardia, or tachycardia; total adverse events were similar for those receiving oral analgesia (5.0%) and those not receiving oral analgesia (5.6%) difference=-0.6% (95% CI -4.7% to 3.9%); results were similar in a secondary analysis of patients receiving oral analgesics within 4 h; the authors did not describe episodes of intubation, aspiration, unplanned admission, or death, although these were not explicit outcome measures in the study	Did not evaluate rationale for some patients receiving oral analgesics and others not receiving oral analgesics; outcome measured with knowledge of oral analgesic administration; it is implied that all of the patients met the department fasting guidelines of 2 h for liquids and 4 h for solids, but this is not explicit; fasting times were similar between groups	II

899

900 **Evidentiary Table (continued).**

Study	Year	Design	Intervention(s)/Test(s)/ Modality	Outcome Measure/Criterion Standard	Results	Limitations/ Comments	Class
Bell et al[30]	2007	Prospective, uncontrolled, observational trial	Single-center study of 400 patients undergoing procedural sedation with propofol; fasting status was evaluated; adult and pediatric patients receiving propofol by protocol with initial bolus of 0.5 mg/kg to 1.0 mg/kg followed by 10-mg to 40-mg bolus doses as needed	Patients not meeting ASA fasting guideline (6 h for solids and 2 h for liquids); patients evaluated for drug dosages administered, NPO status, and adverse events, including emesis	282/400 (70.5%) did not meet fasting guidelines for solids or liquids; emesis occurred in 1/282 (0.4%) of those who did not meet fasting guidelines compared with 1/118 (0.8%) in those who met guidelines, difference=0.4% (95% CI -2.3% to 1.3%);* respiratory adverse events occurred in 63/282 (22.4%) of those who did not meet fasting guidelines compared with 23/118 (19.5%) of those who met guidelines, difference=2.8% (95% CI -5.8% to 11.5%);* respiratory interventions occurred in 94/282 (33.3%) of those who did not meet fasting guidelines compared with 29/118 (24.6%) of those who met guidelines, difference=8.8% (95% CI -0.8% to18.3%);* there were no aspiration events, intubations, LMA insertions, or unplanned admissions related to sedation or recovery in either group (0%, 95% CI 0% to 0.9%)*	Not powered to detect a difference in emesis rate; further design limitations included nonblinded, nonrandomized enrollment, with no comparative group; premedication not standardized; enrollment of patients limited by physician selection bias and convenience	II for fasting III for agents

901 *Calculations of 95% CI and difference in proportions were performed in Stata version11.2 when not reported in the original article.

902 **Evidentiary Table (continued).**

Study	Year	Design	Intervention(s)/Test(s)/ Modality	Outcome Measure/Criterion Standard	Results	Limitations/ Comments	Class
Lightdale et al[31]	2006	Randomized controlled trial	Capnographic measures of hypoventilation used to alert providers at 15 s vs 60 s; pediatric endoscopy with supplemental O_2	Primary outcome was hypoxia defined as pulse oximetry <95% for >5 s; secondary outcomes included abnormal ventilation, termination of procedure, BVM, sedation reversals, or seizures	163 patients with 11% vs 24% of patients with hypoxia in the 15 s vs 60 s arms, respectively; ARR=13% RRR=54% NNT=7.7	Unable to blind; generalizability	II
Qadeer et al[32]	2009	Randomized controlled trial	Capnography vs blinded to capnography results during procedural sedation with opioid and benzodiazepine during ERCP and EUS	Primary outcome: hypoxia defined as O_2 saturation <90% for $\geq$15 s; secondary outcomes: severe hypoxia $\leq$85%; supplemental O_2 use, apnea $\geq$15 s; and abnormal ventilation defined as capnography flat line for $\geq$5 s but <15 s, >75% reduction in amplitude of respiratory waves for $\geq$5 s	263 patients enrolled with similar patients characteristics in each arm; 85 patients (69%) from the blinded arm and 57 (46%) from the open arm developed at least 1 episode of hypoxia; ARR=23% RRR=33% NNT=4.3	Generalizability of results from a study on ERCP and EUS to ED procedural sedation; incorporation bias was important for secondary outcomes only	II

903

Evidentiary Table (continued).

Study	Year	Design	Intervention(s)/Test(s)/ Modality	Outcome Measure/Criterion Standard	Results	Limitations/ Comments	Class
Deitch et al[33]	2010	Randomized controlled trial	Capnography vs no access to capnography by the provider in ED procedural sedation with propofol and supplemental O_2	The primary outcome was hypoxia defined as SpO_2 <93%; respiratory depression was defined as $ETCO_2$ >50 mm Hg, change from baseline of $\geq$10%, or loss wave form >15 s	132 patients with 25% vs 42% patients with hypoxia in the capnography and no capnography arm, respectively; ARR=17%; RRR=59% NNT=5.9	Single center; incorporation bias; unable to blind; 35% excluded because of missing data without sensitivity analysis	II
Waugh et al[34]	2011	Meta-analysis of prospective studies	Capnography in addition to standard monitoring in procedural sedation	Respiratory complications	Five studies included in this systematic review; respiratory events as defined by the various studies were 17.6 times more likely to be detected (95% CI 2.5 to 122) by capnography compared with standard monitoring alone	There was significant heterogeneity in these results, with an I^2(%) of 85.2; generalizability because not all of these studies occurred in the ED setting; 4 of the 5 studies were Class III evidence and 1 study was level X	III
Miner et al[35]	2002	Prospective observational	This study prospectively evaluated the ability of $ETCO_2$ to detect respiratory depression in ED procedural sedation with various agents	Respiratory depression was defined as: oxygen saturation <90% for $\geq$1 min; $ETCO_2$ >50 mm Hg; absent waveform/airway obstruction measured by $ETCO_2$; secondary outcome was ventilatory assistance	74 patients, with 14.9% meeting criteria for respiratory depression; 33% of these were detected by pulse oximetry and 100% were detected by $ETCO_2$ criteria	Single center; small numbers	III

906 **Evidentiary Table (continued).**

Study	Year	Design	Intervention(s)/Test(s)/ Modality	Outcome Measure/Criterion Standard	Results	Limitations/ Comments	Class
Burton et al[36]	2006	Prospective observational	Detection of acute respiratory events with $ETCO_2$ compared with pulse oximetry or clinical examination	Acute respiratory event: $SpO_2 \leq 92\%$, increased O_2 use, BVM, oral/nasal airway, repositioning, or stimulation	60 patients with 20 (33%) acute respiratory events; 17/20 (85%) detected by $ETCO_2$; 70% (95% CI 58% to 82%) $ETCO_2$ before pulse oximetry	Single-center design; convenience sample; incorporation bias; study ended early; not all of these outcomes are likely to be clinically important	III
Deitch et al[37]	2008	Randomized controlled trial of supplemental O_2 vs room air	Supplemental O_2 vs room air to reduce hypoxia in ED procedural sedation with propofol; evaluation of blinded capnography in detecting respiratory depression compared with physician assessment was a secondary hypothesis of the trial	Primary outcome was hypoxia defined as oxygen saturation $\geq 93\%$; secondary outcome was detection of respiratory depression defined as hypoxia, $ETCO_2$ >10 mm Hg from baseline or loss of $ETCO_2$ waveform	110 patients; 52 with respiratory depression; 9 with both hypoxia and respiratory depression criteria, 16 with only hypoxia, and 27 with only $ETCO_2$ criteria	Single center; incorporation bias; not the primary hypothesis of study	III
Vargo et al[38]	2002	Prospective blinded observational	Provider observation vs pulse oximetry <90% vs capnography >25% difference from baseline value in GI endoscopy	Outcomes: apnea >30 s; disordered respiration defined as 45 s containing 30 s of apnea; alveolar hypoventilation defined as $ETCO_2$ $\geq 25\%$ baseline value; and hypoxia defined as pulse oximetry <90%	49 patients enrolled; 54 episodes of disordered respiration in 28 patients; 50% detected by pulse oximetry, 0% by observation, and 100% by capnography	Generalizability; incorporation bias	III

907

908 **Evidentiary Table (continued).**

Study	Year	Design	Intervention(s)/Test(s)/ Modality	Outcome Measure/Criterion Standard	Results	Limitations/ Comments	Class
Deitch et al[43]	2007	Randomized controlled trial	Supplemental O_2 vs room air to reduce hypoxia in ED procedural sedation with midazolam and fentanyl; evaluation of blinded capnography in detecting respiratory depression compared with physician assessment was a secondary hypothesis of the trial	Primary outcome was hypoxia defined as oxygen saturation <90%; secondary outcome of respiratory depression was defined as hypoxia, $ETCO_2$ change of >10 mm Hg from baseline, or loss of $ETCO_2$ waveform	80 patients, 11 with hypoxia and 28 with respiratory depression; physicians detected 0 of 28 with respiratory depression, but no adverse events	Single center; incorporation bias in the definition of respiratory depression; evaluation of capnography was not the primary hypothesis of the study	III
Deitch et al[44]	2011	Randomized controlled trial	High-flow O_2 vs room air to reduce hypoxia in ED procedural sedation with midazolam and fentanyl; evaluation of blinded capnography in detecting respiratory depression compared with physician assessment was a secondary hypothesis of the trial	Primary outcome was hypoxia defined as oxygen saturation <93%; secondary outcome of respiratory depression was defined as $ETCO_2$ change of >50 mm Hg, >10 mm Hg change from baseline, or loss of $ETCO_2$ waveform	117 patients analyzed; 58 patients developed respiratory depression and only 29 of these developed hypoxia	Single center; incorporation bias in the definition of respiratory depression; evaluation of capnography was not the primary hypothesis of the study	III

909

Evidentiary Table (continued).

Study	Year	Design	Intervention(s)/Test(s)/ Modality	Outcome Measure/Criterion Standard	Results	Limitations/ Comments	Class
Anderson et al[45]	2007	Prospective observational study; pediatric orthopedic procedures	Detection of apnea or airway obstruction with capnography compared with pulse oximetry or clinical examination in patients receiving opioid and propofol, as well as supplemental O_2	First to detect adverse respiratory events: hypoxia, hypercarbia, or apnea; hypoxia was defined as oxygen saturation <90% at 4,330 feet elevation; hypercarbia was $ETCO_2$ >50 mm Hg or >10% increase from baseline; apnea was defined as cessation of spontaneous breathing >30 s or absent CO_2 waveform	125 patients enrolled and 14 adverse airway or respiratory events; apnea (5/5) was detected by capnography before pulse oximetry; airway obstruction (6/10) was detected by capnography before pulse oximetry	Single-center design; limited to children; convenience sample; no blinding; incorporation bias because $ETCO_2$ was used in the definition of adverse respiratory events	III
Sivilotti et al[46]	2010	Prospective observational nested in a randomized controlled trial	Capnography vs pulse oximetry in first detection of respiratory depression; this study was nested in a randomized controlled trial of propofol sedation with either low-dose ketamine or fentanyl	Composite endpoint of respiratory events includes oxygen desaturation <92% and hypoventilation defined as $ETCO_2$ >50 mm Hg, a rise of 10 mm Hg from baseline, or loss of waveform	63 patients were enrolled and 36 (57%) developed O_2 desaturation at some point; hypoventilation was associated with hypoxia crude OR=1.4; hypoventilation did not precede hypoxia in any patient	Study was not designed to answer this clinical question; incorporation bias for all outcomes	III

912 **Evidentiary Table (continued).**

Study	Year	Design	Intervention(s)/Test(s)/ Modality	Outcome Measure/Criterion Standard	Results	Limitations/ Comments	Class
Sacchetti et al[58]	2007	Retrospective review of prospective database	Procedural sedation and analgesia with physician doing both sedation and procedure vs physician doing only sedation	Complication rate including airway obstruction, apnea, hypotension, and hypoxia	N=1,028; sedation on 980 patients; complication rate: physician doing sedation and procedure=4.1%, physician doing sedation only=4.0% (*P*>.9)	Did not define procedural sedation; excluded sedation cases performed in ED but not under the direction of the emergency physician; did not control for when the physician performed sedation only vs sedation and procedure; did not assess for differences in patient comorbidities or severity of illness	III
Hogan et al[59]	2006	Retrospective review of prospective database	Procedural sedation and analgesia by single emergency physician with monitoring by emergency nurse vs monitoring by additional emergency physician	Complication rate including airway obstruction, apnea, hypotension, and hypoxia	N=1,028; sedation on 980 patients; complication rate: nurse monitored=4.0%, physician monitored=4.2%; *P*>.7)	Did not prospectively determine when nurse monitoring or physician monitoring should apply	III

913

Evidentiary Table (continued).

Study	Year	Design	Intervention(s)/Test(s)/ Modality	Outcome Measure/Criterion Standard	Results	Limitations/ Comments	Class
Vinson and Hoehn[60]	2013	Retrospective, consecutive multicenter case series	1 physician and 1 nurse vs 2 physicians and 1 nurse procedural sedation and analgesia in ED patients requiring closed reduction of major joint dislocations and forearm fractures	Incidence of success of the procedure and adverse events requiring intervention	In 98.4% (435/442) patients, a single emergency physician simultaneously managed both the procedural sedation and the initial orthopedic reduction without the assistance of a second physician; the reduction was successful or satisfactory in 96.6% (425/435) (95% CI 95.8% to 98.8%) of these cases, with a low incidence of intervention-requiring adverse events (2.8% [12/435]; 95% CI 1.5% to 4.8%); adverse events requiring intervention occurred in 12 (2.8%) of 435 cases using the 1 physician and 1 nurse model and in none of the 22 cases with 2 physicians and 1 nurse (*P*=.43)	Retrospective chart review; small numbers (N=22) of cases using 2 physicians for procedural sedation and analgesia; focused solely on orthopedic procedures so generalizability to other procedural sedation and analgesia indications is limited	III
Kuypers et al[64]	2011	Prospective, uncontrolled, multicenter observational trial	Adult and pediatric patients receiving propofol by protocol with initial bolus of 0.5 mg/kg followed by repeated bolus doses as needed; IV fentanyl administered before propofol at the discretion of the attending physician	Patients evaluated for drug dosages administered, quality of sedation, and adverse events	386 patients received propofol, with a median dose of 1.0 mg/kg; 99.5% of procedures were successful; majority of patients with either dislocation reduction or electrical cardioversion; complications included apnea in 11%; BVM use not reported, hypoxia in 5%, hypotension in 3%; vomiting noted in 1 patient	Design limitations included nonblinded, nonrandomized enrollment, with no comparative group; premedication not standardized; enrollment of patients limited by physician selection bias and convenience	III

Evidentiary Table (continued).

Study	Year	Design	Intervention(s)/Test(s)/ Modality	Outcome Measure/Criterion Standard	Results	Limitations/ Comments	Class
Senula et al[65]	2010	Prospective, controlled, nonrandomized, single-center observational trial	Adult and pediatric patients receiving procedural sedation before and after introduction of propofol to ED formulary	Primary outcome variable was the frequency of propofol use for sedation; secondary variables included the rate of predefined observed respiratory depression, efficacy, and duration of recovery	573 subjects enrolled and analyzed, with 255 enrolled before propofol use and 318 enrolled after propofol introduction; baseline characteristics were similar between groups except for more male patients and more children in the postpropofol group; sedation performed primarily for orthopedic procedures; complications and procedure failures decreased after propofol introduction; propofol use increased with time in the postpropofol period	Flaws in design	III

Evidentiary Table (continued).

Study	Year	Design	Intervention(s)/Test(s)/ Modality	Outcome Measure/Criterion Standard	Results	Limitations/ Comments	Class
Miner et al[66]	2009	Nonblinded, randomized, controlled study	Adult patients treated with IV morphine for analgesia by protocol and then randomized to treatment protocol with propofol 1.0 mg/kg bolus accompanied by either placebo or alfentanil 10 µg/kg	Primary outcome variables included depth of sedation, rate of predefined observed respiratory depression, efficacy, and duration of recovery; the secondary objective was to compare rates of clinical vs subclinical respiratory depression rates	145 patients enrolled and analyzed, with 74 randomized to receive placebo and 71 to alfentanil treatment; baseline characteristics were similar between groups; no significant difference was observed in adverse respiratory events between groups except for patients requiring stimulation to induce breathing to resolve hypoventilation, with more patients requiring stimulus in the alfentanil group; procedure success was similar between groups; recovery times were longer in alfentanil-treated patients	Nonblinded to patients and providers	II

Evidentiary Table (continued).

Study	Year	Design	Intervention(s)/Test(s)/ Modality	Outcome Measure/Criterion Standard	Results	Limitations/ Comments	Class
Miner et al[83]	2007	Nonblinded, randomized, controlled study	Adult patients treated with IV morphine for analgesia by protocol and then randomized to treatment protocol with either etomidate or propofol administered by treatment protocol; propofol administered as 1.0 mg/kg bolus followed by 0.5 mg/kg bolus doses as needed; etomidate administered as 0.1 mg/kg followed by 0.05 mg/kg bolus as needed	Outcome variables included the rate of predefined, observed respiratory depression, efficacy, and duration of recovery	214 patients enrolled and analyzed, with 105 randomized to receive etomidate and 109 to propofol treatment; baseline characteristics were similar between groups; myoclonus noted in 20% of etomidate patients, 1.8% of propofol patients; no significant difference observed in adverse respiratory events between groups, including BVM used in 3.8% of etomidate and 4.6% of propofol patients; procedure success was more common in the propofol-treated patients; recovery times were similar in the 2 groups; sedation performed primarily for orthopedic and incision and drainage procedures	Nonblinded to patients and providers	II

ARR, absolute risk reduction; *ASA*, American Society of Anesthesiologists; *BVM*, bag-valve-mask; *CI*, confidence interval; CO_2, carbon dioxide; *ED*, emergency department; *ERCP*, endoscopic retrograde cholangiopancreatography; $ETCO_2$, end-tidal carbon dioxide; *EUS*, endoscopic ultrasonography; *GI*, gastrointestinal; *h*, hour; *Hg*, mercury; *IV*, intravenous; *kg*, kilogram; *LMA*, laryngeal mask airway; *µg*, microgram; *mg*, milligram; *min*, minute; *ml*, milliliter; *mm*; millimeter; *NNT*, number needed to treat; *NPO*, nothing by mouth; O_2, oxygen; *OR*, odds ratio; *RRR*, relative risk reduction; *s*, seconds; SpO_2, oxygen saturation; *vs*, versus; *y*, year.

Appendix A. Literature classification schema.*

Design/ Class	Therapy†	Diagnosis‡	Prognosis§
1	Randomized, controlled trial or meta-analysis of randomized trials	Prospective cohort using a criterion standard or meta-analysis of prospective studies	Population prospective cohort or meta-analysis of prospective studies
2	Nonrandomized trial	Retrospective observational	Retrospective cohort Case control
3	Case series Case report Other (eg, consensus, review)	Case series Case report Other (eg, consensus, review)	Case series Case report Other (eg, consensus, review)

*Some designs (eg, surveys) will not fit this schema and should be assessed individually.
†Objective is to measure therapeutic efficacy comparing interventions.
‡Objective is to determine the sensitivity and specificity of diagnostic tests.
§Objective is to predict outcome including mortality and morbidity.

Appendix B. Approach to downgrading strength of evidence.

	Design/Class		
Downgrading	**1**	**2**	**3**
None	I	II	III
1 level	II	III	X
2 levels	III	X	X
Fatally flawed	X	X	X

Appendix C. Likelihood ratios and number needed to treat.*

LR (+)	LR (-)	
1.0	1.0	Useless
1-5	0.5-1	Rarely of value, only minimally changes pretest probability
10	0.1	Worthwhile test, may be diagnostic if the result is concordant with pretest probability
20	0.05	Strong test, usually diagnostic
100	0.01	Very accurate test, almost always diagnostic even in the setting of low or high pretest probability

LR, likelihood ratio.
*Number needed to treat (NNT): number of patients who need to be treated to achieve 1 additional good outcome; NNT=1/absolute risk reductionx100, where absolute risk reduction is the risk difference between 2 event rates (ie, experimental and control groups).