Discussion

Etomidate is one of several intravenous agents (e.g., propofol, methohexital, and ketamine) that are administered to induce general anesthesia when given in doses higher than those administered for sedation. Etomidate has become one of the most common induction agents administered in the emergency department as part of rapid-sequence intubation. Its popularity is likely due to its rapid onset and offset, minimal histamine release, and stable hemodynamic profile.[18-21]
We defined recovery as a return to full response to verbal commands because this was clearly marked on the sedation logs. We could not determine exactly at what point the patients met standard discharge criteria. Nor did we compare recovery times in this study with those for other agents (e.g., midazolam).

Level of Sedation

The key feature of general anesthesia induced by the potent intravenous sedative agents is complete loss of consciousness (not responsive to painful stimulation), whereby patients lose the ability to maintain a patent airway.[22] Deep sedation has been defined as a depressed consciousness from which patients are not easily aroused and do not respond purposefully to stimuli. Such patients may have partial or complete loss of protective airway reflexes.[23,24]
Therefore, the distinction between general anesthesia and deep sedation may be subtle when administering sedative agents in the clinical setting due to interpatient and intrapatient variability in drug disposition. Administration of these potent intravenous sedatives by emergency physicians and other nonanesthesiologists has been controversial[24] despite the increasing number of reports of their administration before patients undergo painful or uncomfortable procedures.[1-17,23-26]
One report of administration of propofol for deep sedation was accompanied by a commentary arguing against the rapid widespread acceptance of this agent in the emergency department.[23,24] Similar concerns have been raised regarding administration of agents such as propofol in other settings, where sedation is induced for procedures such as gastrointestinal endoscopy.[27] Some of these concerns stem from the lack of a widely accepted method of monitoring or quantifying depth of sedation beyond a patient's ability to respond to verbal, tactile, or painful stimuli. The bispectral index monitor (Aspect Medical Systems, Natick, MA), a device that offers an objective measurement of sedation using bispectral electroencephalography, may better define the borders between sedation levels.[28,29]

Lack of Guidelines

Despite the growing number of reports regarding potent intravenous sedatives for various procedures, few published guidelines specifically address administration of etomidate (or similar intravenous sedatives) in the emergency department. This lack of guidelines is partially a function of investigations published during the last few years. For example, reviews[30] and consensus guidelines[26,31] discussing the pharmacology of pain and sedation management in the emergency department have not mentioned etomidate, although they discuss ketamine and propofol. This is not surprising because the reports concerning etomidate administration in the emergency department were published after 1999.[11-17]
Another explanation for the lack of applicable guidelines concerning etomidate for sedation in the emergency department pertains to the controversy regarding personnel (who should administer the sedative) and setting (where various levels of sedation should be provided). The Joint Commission on Accreditation of Healthcare Organizations (JCAHO) does not detail the administration of specific drugs by clinicians in specific hospital settings. Whereas the JCAHO acknowledges the continuum of the sedation-to-anesthesia process, it distinguishes moderate sedation-analgesia (previously referred to as conscious sedation) and deep sedation-analgesia

based on patient arousability and ability to maintain spontaneous ventilation.[32] The JCAHO standards state that practitioners administering deep sedation must have appropriate credentials, including the ability to recover patients from general anesthesia.

Similar to JCAHO standards, sedation guidelines established by groups such as the American Society of Anesthesiologists (ASA), the Canadian Association of Emergency Physicians, and the North American Society for Pacing and Electrophysiology (NASPE) focus on monitoring, personnel, equipment, and discharge issues relative to sedation procedures.[25,26,33] Rather than detail the administration of drugs, these guidelines involve general principles related to sedative titration and administration of reversal agents. Furthermore, these organizational guidelines do not discuss the qualifications of personnel needed to titrate these agents to a particular level of sedation (i.e., moderate vs deep sedation). The ASA guidelines specifically exclude situations in which the level of sedation would "...eradicate the purposeful response to verbal commands or tactile stimulation."[25] Similarly, the NASPE consensus guidelines state that deep sedation is beyond the scope of the document since it requires anesthesia services.[33] Although these published guidelines do not address deep sedation specifically, some institutions (including ours) have determined that incorporating this issue in their institutional guidelines is appropriate.[34]

Complications

Safety concerns are at the root of many arguments against the administration of potent intravenous sedatives such as propofol and etomidate in the emergency department, particularly with the lack of available reversal agents.[24,27] Although etomidate is associated with little respiratory depression,[35] two patients in our series had respiratory complications. This may overestimate the true frequency because both had received adjunctive opiates, and one also received benzodiazepine. A series of 53 children receiving etomidate sedation for fracture reduction reported no episodes of apnea or desaturation.[13] A recent report involving 40 sedations, in which etomidate was administered as a single agent, found no episodes of respiratory depression or emesis.[17] However, a series of 51 patients who received etomidate sedation reported desaturation in 10% of patients.[12] Transient hypoxemia has been reported in 1-12% of patients receiving midazolam, propofol, and methohexital for procedural sedation.[1,2,7,8,14,23,30] It remains unclear, therefore, whether, and to what extent, respiratory depression occurs with etomidate sedation.
Nausea, vomiting, and myoclonus are other adverse effects that have occurred with etomidate administration.[6,8,13,15,36] Emesis occurred in two (4%) of our patients without evident aspiration. No myoclonus was noted in our patients, but this may have been due to the perception by our emergency department physicians of the benign nature of the myoclonic movements, the fact that the study was retrospective, or the high frequency of adjunctive drugs given. Also, our practice of administering etomidate relatively slowly may have resulted in less myoclonus. Etomidate-associated myoclonus occurs in 0-80% of patients and is considered dose related.[6,8,13,36] Emergence anxiety, which has not been well described, occurred in two of our patients after especially painful procedures (chest tube insertion). This complication may have been the result of inadequate analgesia.

A major concern related to etomidate admin-istration is the possibility of adrenal suppression. Etomidate inhibits 11-b-hydroxylase, an enzyme that promotes conversion of 11-deoxycortisol to cortisol.[37,38] Although a cause-and-effect relationship was never established, adrenal suppression was postulated as the mechanism responsible for the increased mortality seen in trauma patients who were given etomidate in the early 1980s outside the United States.[39,40] Although no clinical signs or symptoms of adrenal suppression were noted in our patients, adrenal function was not tested. Most reports on adrenocortical suppression have involved patients sedated with continuous infusion.[39-42] However, decreased plasma cortisol levels have been reported after a single induction dose.[43-47] One prospective, randomized study investigated the effects on adrenocortical function in patients in the emergency department receiving one dose of intravenous etomidate 0.3 mg/kg for intubation.[16] Suppression in cortisol response was

statistically significant based on a 4-hour cosyntropin stimulation test (100% normal response in controls vs 30% in the etomidate group, p=0.004) but not the 12- or 24-hour tests. However, all cortisol concentrations in the etomidate group were within the normal laboratory range, and no clinical sequelae were noted. The data thus far indicate that adrenal axis dysfunction occurs with single doses but likely resolves in 4-8 hours. No evidence has indicated that adverse clinical outcomes result from this dysfunction.

Concerns

Our emergency department staff have attempted to proactively address local concerns as well as concerns raised in the literature[24] relative to administration of potent intravenous sedatives by emergency department physicians. Our physicians requested and were granted privileges for administration of intravenous parenteral general anesthetic agents based on a number of measures that have been taken to ensure appropriate education and training. A focused education curriculum covering the practice of deep sedation is provided to all emergency department physicians by residency-trained, board-certified emergency physicians who have the skills and knowledge needed to practice and teach the principles of deep sedation. A deep-sedation protocol has been created based on protocols administered by anesthesiologists for monitored anesthesia care.[25,26] A hospitalwide sedation policy consistent with this protocol is in place. It requires that a separate sedating physician is present, monitoring is similar to the level administered in the operating room, and operational resuscitation equipment is at bedside. As a result of ongoing reviews, a more stringent protocol has been instituted for administration of etomidate, including strict fasting times (6-8 hours for solids and nonclear liquids and 2-3 hours for clear liquids).[25] Finally, we have instituted a method of tracking adverse events to allow real-time follow-up with involved physicians and to identify sentinel events that may occur.

Limitations of the Study

The most significant limitations of our study result from its retrospective design. Also, adverse events may not have been reported because the health care professionals may not have related an event to the drug unless it was obvious in the time sequence. In addition, long-term follow-up to monitor patients for possible delayed adverse events did not occur. Finally, the frequent administration of adjunctive drugs is another confounding variable that makes it difficult to evaluate safety and efficacy solely attributable to etomidate.