Sedation: Not Quite That Simple

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In recent years, the number of diagnostic and surgical procedures performed with sedation has increased exponentially, with the majority of the growth occurring in ambulatory surgical centers, physicians’ offices, and hospital locations outside the operating room (also referred to as remote locations). Sedation and analgesia minimize patient anxiety and discomfort, and allow patients to remain immobile for the procedure. Other benefits include the avoidance of airway interventions, as well as general anesthesia and its associated complications. Furthermore, sedation/analgesia facilitates and expedites procedures and allows early recovery and discharge. Sedation provides for a superior patient experience that may improve overall patient satisfaction. However, sedation/analgesia techniques can be associated with significant adverse events that might increase morbidity and mortality.

This article reviews the complications associated with sedation/analgesia techniques and provides an approach for their safe administration, and discusses the newer drugs and devices used for provision of sedation/analgesia.

COMPLICATIONS ASSOCIATED WITH SEDATION/ANALGESIA TECHNIQUES

The overall complication rate associated with sedation/analgesia techniques remains unknown because the literature is sparse and of limited quality. Nevertheless, it is well accepted that although the mortality of sedation is low, the associated morbidity can be significant. Complications of sedation/analgesia include respiratory complications such as loss of airway patency, airway obstruction, and respiratory depression. That may lead to life-threatening hypoxia and hypercarbia as well as cardiovascular complications such as hypotension and cardiac arrhythmias. In addition, depression of protective airway reflexes during excessive sedation can lead to an unprotected airway and thereby increase the risk regurgitation and aspiration of gastric contents. The risks inherent in the procedures as well as risk of patient movement that may
be detrimental to the patient should also be taken into consideration. Another concern, although rare, is the potential for drug interactions or adverse reactions, including anaphylaxis. Of note, residual sedative effects have the potential to cause delayed complications (eg, hypoxia after discharge) that can be hazardous to unsupervised patients.

Analysis of the American Society of Anesthesiologists (ASA) closed claim database of monitored anesthesia care (MAC) cases found that more than 40% of claims associated with MAC involved death or permanent brain damage, and the incidence was similar to claims associated with general anesthesia. Respiratory depression with hypoventilation after absolute or relative overdose of sedative-hypnotics and/or opioids was the most common mechanism of injury. The investigators reviewing these claims concluded that nearly 50% of complications were preventable.

Another analysis by Metzner and colleagues of the ASA closed claims database, comparing liability in the operating room with that in remote locations (eg, gastrointestinal suite, interventional cardiology suite, interventional radiology suite, and magnetic resonance imaging suite), found that 50% of remote location liability claims involved MAC. The proportion of claims of death was higher in remote locations than in the operating room. Inadequate oxygenation/ventilation secondary to oversedation accounted for more than a third of the claims. In addition, sedation in the prone position, for example, during endoscopic retrograde cholangiopancreatography (ERCP), may further increase the complication rate due to difficulty in securing the airway and resuming adequate ventilation. Similar to the previous report, this study also determined that better monitoring could have prevented the substandard care that led to complications. These investigators emphasize that monitoring standards and guidelines used for general anesthesia should be used for sedation care outside the operating room.

A recent study evaluated the safety and efficacy of propofol/opioid sedation, administered by anesthesia providers, for advanced endoscopic procedures that require deep sedation (eg, ERCP and endoscopic ultrasound). In this study of 799 patients, airway manipulations were required in 14.4% of cases. The incidence of hypoxemia was 12.8%, hypotension occurred in 0.5%, and premature termination of the procedure was required in 0.6% of patients. No patient required bag-mask ventilation or tracheal intubation. Predictors of airway manipulation included male gender, higher body mass index (weight in kilograms divided by height in meters squared), and ASA physical status of 3 or higher. The dose of propofol used in this study was similar to that required for provision of general anesthesia. The propofol dose to induce sedation was 2.41 ± 1.13 mg/kg when used alone and 1.37 ± 0.75 mg/kg when used in combination with opioids, while the propofol dose used for maintenance of sedation was 0.23 ± 0.1 mg/kg/min when used alone and 0.17 ± 0.11 mg/kg/min when used in combination with opioids. In addition, 87.2% of patients had no response to insertion of the endoscope, which also suggests that the patients experienced deep sedation or general anesthesia. Thus, the procedures were essentially performed under general anesthesia (ie, total intravenous anesthesia) without tracheal intubation. Therefore, this study questions the routine use of general anesthesia with tracheal intubation for patients undergoing advanced gastrointestinal endoscopic procedures, which is in contrast to the recommendation by Metzner and colleagues.

An analysis of patients developing apnea and cardiopulmonary arrest during and after endoscopy found that the majority of complications occurred around the time of drug administration or after the procedure had ended, usually around 30 minutes after the last dose of sedative-hypnotic and/or opioid administration. The investigators also reported that although pulse oximetry did not reduce the complication
rate, it allowed early recognition of apnea and cardiopulmonary arrest. This study emphasizes that postsedation observation is critical, particularly in the elderly and patients with comorbidities.

In recent years, there has been an increasing trend toward propofol use by nonanesthesia practitioners, including registered nurses, which has become a subject of major controversy. The safety of nonanesthesia practitioner administered propofol (NAAP) was observed in 646,080 patients undergoing gastrointestinal endoscopic procedures. These observational studies reported a low complication rate, which included the need for tracheal intubation in 11 patients and death in 4 patients, but no patient who survived had any permanent neurologic injury. Mask ventilation was required in 0.1% cases. Overall, the safety of NAAP for upper endoscopy and colonoscopy is the same as that of a benzodiazepine/opioid technique. Of note, the reported mortality with a conventional benzodiazepine and opioid combination is 11 deaths per 100,000 cases. A recent study reported that deep sedation frequently occurred with midazolam/meperidine sedation during endoscopic sedation.

A position statement by the American Association for the Study of Liver Diseases, the American College of Gastroenterology, the American Gastroenterological Association Institute, and the American Society for Gastrointestinal Endoscopy claims that the safety profile of NAAP is equivalent to that of standard benzodiazepine/opioid sedation. It must be noted, however, that the majority of the observational trials included in the evaluation of the safety of NAAP sedation are from a select few endoscopic units with extensive experience. Also, the sedation for endoscopy was provided by the sole use of propofol. It is likely that the complication rate may increase if propofol is used in combination with benzodiazepines and/or opioids, which is usually necessary for more painful procedures. Furthermore, there is a paucity of data on the safety of propofol administered by nonanesthesia practitioners for procedures other than gastrointestinal endoscopies. Therefore, widespread indiscriminate use of propofol by non-anesthesia practitioner may compromise patient safety.

In an interesting editorial endorsing the use of propofol in the emergency unit, Green and Krauss identified risk of aspiration as the most serious risk rather than airway obstruction and respiratory depression. Green and Krauss recommended clinicians to “avoid assisting ventilations” and to “simply ‘wait out’ an occurrence of propofol-associated respiratory depression” so as to minimize the risk of aspiration. Such statements obviously confirm that these investigators, who are supposed to be experts on sedation in the emergency unit, lack the understanding of risks associated with propofol use. Similarly, a recent article on nurse-administered propofol sedation for gastrointestinal endoscopic procedures states that “when using a multidrug protocol with propofol, the clinician may be able to exploit the therapeutic actions of the individual agents while reducing the possibility of sedation dose-related complications.” This standpoint is contrary to the established principles of polypharmacy emphasizing that the risk of hypoxia, hypercarbia, and airway compromise are actually worsened when propofol is combined with benzodiazepines and/or opioids. A lack of appreciation for the risks associated with sedation and inappropriate management of complications will lead to increased morbidity and mortality.

FACTORS INFLUENCING SEDATION-RELATED COMPLICATIONS

Some of the factors that influence sedation/analgesia complications include patient characteristics, type of procedure, drug selection and dosing, monitoring, and training. Patient characteristics that influence sedation-related complications include extremes of age, significant airway abnormalities, obstructive sleep apnea (OSA),
morbid obesity, and ASA physical status of 3 or greater. The increased risk of developing complications in this patient population is due to increased sensitivity to sedative-hypnotics and opioids and/or altered pharmacokinetics and drug clearance. Similarly, certain types of procedures (eg, those requiring deeper levels of sedation to prevent patient movement) may not be suitable for sedation/analgesia, and it may be safer to perform them using general anesthesia. Also, the frequency of complications may be influenced by expectations of deeper levels of sedation by patients and proceduralists.

Achieving an appropriate level of sedation remains a clinical challenge, as sedation represents a continuum of progressive impairment of consciousness that extends from wakefulness to general anesthesia. As the patient transitions between stages, they clearly become subject to respiratory and cardiovascular complications. Because of wide variability in patient response to sedative regimens, the appropriate dosage needed to achieve a specific level of sedation cannot always be predicted. Another factor that might influence the complication rate is the synergistic effects of combinations of sedative-hypnotics and opioids as well as the accumulation of active metabolites (eg, midazolam). Lysakowski and colleagues administered opioids to achieve a specific effect-site concentration (fentanyl, 1.5 ng/mL; alfentanil, 100 ng/mL; remifentanil, 6 ng/mL; and sufentanil, 0.2 ng/mL; or placebo) to a group of patients who then received propofol infusions. At the time of loss of consciousness (LOC), the effect-site concentration of propofol was recorded. The investigators found that, compared with placebo, patients who had received any of the 4 opioids achieved LOC at lower propofol concentrations. Training and skills, patient selection, including identification of patients and procedures that may be more safely performed by using a general anesthetic, and monitoring and vigilance also influence the sedation-related complication rate.

SAFE USE OF SEDATION AND ANALGESIA TECHNIQUES

The goals of a sedation/analgesia technique require a balance between patient comfort and safety (ie, avoidance of respiratory and cardiovascular adverse effects and delayed recovery and discharge home). It is important that the patient is prepared appropriately and is not promised total amnesia, sleep, and oblivion, or complete absence of pain. The level of sedation must be coupled with the invasiveness of the procedure as well as the anxiety and cooperation of the patient. Sedative-hypnotics and opioids should be administered prior to the noxious stimuli, rather than at the time of the stimulus, as they have slow blood-brain equilibrium times. In fact, drug administration at the time of the noxious stimuli may result in inadvertent overdosing. Similarly, drug boluses should be adequately spaced, based on the time to peak effect, to avoid overdosing. Furthermore, it is important to avoid using deeper levels of sedation to compensate for inadequate analgesia.

Many professional associations have recently published sedation guidelines to ensure high standards of patient care. The guidelines include recommendations for preprocedure evaluation and selection, sedation techniques, monitoring, recovery, and discharge protocols as well as the availability of appropriate facilities, equipment, staffing, and training.

SEDATIVE-HYPNOTIC MEDICATIONS

Although several medication options exist, sedation in adults is typically achieved by a combination of benzodiazepines (eg, midazolam) and opioids (eg, meperidine or fentanyl). Midazolam provides reliable anxiolysis, sedation, and amnesia as well as
centrally mediated muscle relaxation. In addition, it has a wide margin of safety and can be quickly reversed by administration of the benzodiazepine antagonist flumazenil. However, midazolam produces a dose-dependent cardiorespiratory depression, which might be further exaggerated due to a synergistic effect when combined with other sedatives and opioids. Another major limitation of midazolam is that it has a slow onset and a prolonged duration that might delay recovery, discharge home, and the return to daily living.32

Propofol

Propofol, an intravenous hypnotic drug with rapid onset and short duration of action, can be used to provide moderate to deep sedation. The rapid onset of action allows early achievement of the desired level of sedation. Because of its short duration of action and lack of accumulation, propofol allows a more rapid recovery of cognitive function. Other benefits of propofol include antiemetic and euphoric effects. Propofol sedation has been associated with improved patient satisfaction compared with benzodiazepine/opioid combinations. Furthermore, propofol reduces recovery room stay (and improves throughput) and allows an early return to daily living. Because of these numerous exceptionally desirable characteristics, propofol has become an attractive option for sedation.

Propofol is, however, associated with hemodynamic effects (eg, hypotension) as well as respiratory depression and airway obstruction. Propofol has no analgesic effects and therefore it may have to be combined with opioids for painful procedures. Concomitant use of propofol and opioids or benzodiazepines can cause significant cardiorespiratory depression. Propofol has a narrow therapeutic range, which may result in a deeper than expected depth of sedation, and it lacks a reversal agent.

Fospropofol

Fospropofol is a water-soluble prodrug of propofol that was recently approved for sedation/analgesia. Fospropofol is metabolized by endothelial alkaline phosphatases to propofol, phosphate, and formaldehyde.33–36 Formaldehyde is readily converted to formate, which is metabolized in the liver to water and carbon dioxide. Although formate toxicity can cause lactate acidosis, this has not been reported even with long-term fospropofol infusion. Fospropofol is formulated in an aqueous solution with some potential benefits over propofol (eg, pain on injection and safety issues related to lipid-containing formulation such as hyperlipidemia and risk of infection). Although fospropofol does not cause pain on injection, a side effect commonly seen with propofol, it has been associated with paresthesias (burning sensations and tingling) in the perianal and perineal area. The mechanism of this is still unknown. However, the paresthesias are usually described as mild in intensity, transient, and self-limited, typically lasting for 1 to 2 minutes. Also, similar to its metabolite, propofol, fospropofol can cause dose-dependent hypotension, respiratory depression, and apnea.33,36

The sedative properties of fospropofol are similar to those of propofol, but with a slower onset and offset.35,36 The slower offset of fospropofol may allow a short procedure (approximately 20–25 minutes) to be performed without repeated dosing. However, clinical experience with fospropofol, particularly in nongastrointestinal procedures, is limited. Also, currently recommended fospropofol dosing is complex and based on its use by nonanesthesia practitioners. Similar to propofol, the US Food and Drug Administration (FDA) approval information and product label state that when used to induce and maintain anesthesia, fospropofol “should
be administered only by persons trained in the administration of general anesthesia.”

**MANAGEMENT OF PROCEDURAL PAIN**

Pain during interventional and invasive procedures can be managed with opioids and/or nonopioid analgesics. The sole use of sedative-hypnotics, which do not have analgesic effects, during painful procedures will require deep sedation and increase the risk of cardiopulmonary complications. Therefore, sedative-hypnotics should not be used to compensate for inadequate analgesia (eg, an inadequate local anesthetic technique). The use of analgesics as adjuncts to hypnotic-sedatives may provide adequate pain relief and reduce the total dose of hypnotic-sedative, but may also increase the incidence of cardiopulmonary complications due to the synergistic effects of combining multiple drug classes.

**Opioids**

Opioids (eg, fentanyl, sufentanil, and remifentanil) are commonly used as adjuncts to sedatives to provide analgesia and reduce the autonomic effects of noxious stimuli. Remifentanil has a short duration of action that does not increase with longer duration of administration because of rapid clearance (elimination half-life of 20–30 minutes context-sensitive half-time is 3–5 minutes) and lack of accumulation. Therefore, remifentanil (0.05–0.5 μg/kg/min) is useful for conscious sedation and allows titratable balance between analgesic and respiratory depressant effects. Although the combination of opioids with hypnotic-sedatives in appropriate doses may be beneficial with respect to recovery and side effect profile, inappropriate doses and combinations may significantly increase the incidence of undesirable side effects such as respiratory depression, hypoxemia, and nausea and vomiting, as well as delay of recovery. It is important that opioids should be avoided or the dose limited in at-risk patient groups such as the elderly, morbidly obese, and those with OSA.

**Ketamine**

Ketamine is a dissociative anesthetic with analgesic properties. Ketamine has cardiovascular-stimulating effects (ie, increased heart rate and blood pressure) but no respiratory-depressive effects. Therefore, combining ketamine (0.25–1 mg/kg) with propofol should reduce propofol requirements and mitigate the respiratory and hemodynamic side effects of propofol. The analgesic effects of ketamine should improve the quality of procedural sedation. Furthermore, ketamine produces positive mood effects with perceptual changes, provides prolonged analgesia that extends into the postprocedure period, and allows earlier recovery of cognitive function.

Despite the potential benefits of a propofol/ketamine combination it is not commonly used, likely due to lack of knowledge about the optimal ketamine dose as well as concerns about ketamine’s side effects. A systematic review of the combination of low-dose ketamine with propofol for procedural sedation/analgesia in the emergency department concluded that a ketamine/propofol combination reduced the incidence of significant hemodynamic and respiratory compromise. The need for active interventions, however, including fluid/vasopressor administration, need for supplemental analgesia, or assisted ventilation, was similar. The time to discharge was also similar. Patients who received higher doses of ketamine had a higher incidence of nausea, vomiting, and emergence reactions after the procedure. Because the total number of patients included in the 11 trials who were
evaluated in the systematic review was small, the investigators concluded that insufficient evidence exists to recommend the routine use of a ketamine/propofol combination for sedation in the emergency department setting.

Ketamine can cause copious secretions that might lead to laryngospasm. In addition, it produces skeletal muscle hypertonus and involuntary purposeful movements. Larger ketamine doses can result in deep sedation or general anesthesia, and associated complications including reduced gag reflex and airway obstruction. Another major concern with ketamine is the potential for emergence reactions manifested by vivid dreams and hallucinations. These complications may be avoided if the dose of ketamine is limited to 0.25 to 0.5 mg/kg boluses with a maximum of 2 mg/kg over a 30-minute period.

**Glucocorticoids**

Glucocorticoids have anti-inflammatory properties and therefore have the potential to reduce the inflammatory response to surgical stress and improve postoperative outcome. Dexamethasone (4–8 mg) causes analgesia and euphoria. Dexamethasone has also been shown to reduce postoperative nausea and vomiting. Thus, the combination of dexamethasone with the sedation/analgesia technique has the potential for improving the quality of procedural sedation. Although no side effects have been observed with a single dose of dexamethasone in large studies, there is a potential for increased gastrointestinal side effects as well as delayed wound healing.

**Dexmedetomidine**

Dexmedetomidine is a centrally acting \( \alpha_2 \) agonist with hypnotic, analgesic, and sympatholytic properties. Dexmedetomidine is gaining popularity for procedural sedation because it has sedative as well as analgesic effects. In addition, it has minimal effects on ventilation. Although it causes a decrease in minute ventilation, similar to that seen during natural sleep, it maintains the normal ventilatory response to hypercarbia. Therefore, dexmedetomidine may be beneficial in select patient populations sensitive to sedative-hypnotics, resulting in life-threatening respiratory depression and airway obstruction (eg, morbidly obese and OSA). A recent study reported that compared with a midazolam/fentanyl sedation technique, a dexmedetomidine bolus of 1 \( \mu \)g/kg over 10 minutes followed by an infusion of 0.2 to 1 \( \mu \)g/kg/h provided superior patient satisfaction, with lower opioid requirements and a lower incidence of respiratory depression. Another study found that dexmedetomidine was less effective than propofol/fentanyl for sedation during ERCP. However, dexmedetomidine can cause bradycardia and hypotension. Hypertension has also been observed with increasing plasma levels. Other limitations of dexmedetomidine include a slow onset and longer duration of action, and a duration of action based on the duration of infusion as well as the infusion rate. In a recent study, 49 patients undergoing outpatient extracorporeal shock wave lithotripsy were randomized to receive dexmedetomidine or midazolam/fentanyl sedation. The investigators found prolonged recovery time (116 vs 51 minutes; \( P < .001 \)) and a greater requirement of rescue midazolam (96% vs 58%; \( P = .002 \)) in the dexmedetomidine group. Avoidance of a bolus dose may reduce the hemodynamic adverse effects. Therefore, an initial infusion rate of 1 \( \mu \)g/kg/h, which is then titrated to a sedation level and/or hemodynamics, is recommended. A combination of ketamine with dexmedetomidine may reduce dexmedetomidine requirements and associated side effects as well as improve procedural sedation.
MONITORING DURING SEDATION AND ANALGESIA

Early detection of upper airway obstruction, respiratory depression, and apnea, which are the most common sedation-related complications, should prevent hypoxia and hypercarbia and associated complications such as permanent brain damage and death. Many critical events could be detected early or avoided entirely by appropriate monitoring, particularly respiratory monitoring.5,6,49

Because the procedures performed under sedation/analgesia are minimally invasive (or relatively noninvasive), one may be lulled into complacency. An inappropriate assumption may be made that the degree of care and vigilance required during sedation could be less intense or less thorough. Signs of airway obstruction include snoring, retraction of the suprasternal notch, and paradoxic pattern of breathing. Monitoring of oxygen saturation has become the standard of care; however, there is a considerable delay between the onset of hypoxemia and the detection of desaturation by a pulse oximeter. This is particularly true in patients receiving supplemental oxygen, which has also become the standard of care during sedation. An analysis of deaths during upper gastrointestinal endoscopy (n = 153) revealed that 88% occurred during sedation while only 56% were monitored with pulse oximetry and none had expired carbon dioxide (CO2) monitoring.50

Monitoring of ventilation during sedation can be accomplished by auscultation of breath sounds using a precordial stethoscope, electrical impedance, or capnography monitoring. Precordial auscultation and electrical impedance monitoring detect respiratory efforts but not upper airway obstruction. In contrast, capnography (ie, monitoring of the exhaled CO2 waveform rather than just the value of end-tidal CO2 concentration) allows early detection of airway obstruction and apnea, and reliably predicts impending hypoxemia.51,52 In a study by Soto and colleagues,51 apnea for more than 20 seconds was detected by capnography but not by clinical signs of obstruction and pulse oximetry. Thus, exhaled CO2 monitoring should be routinely used during moderate to deep sedation.

SUPPLEMENTAL OXYGEN

Supplemental oxygenation prolongs the time to desaturation.53 Supplemental oxygen increases oxygen reserves and decreases the likelihood of hypoxemia, thus providing an additional margin of safety. However, this may provide a false sense of security, and delay the diagnosis of airway obstruction and respiratory depression. Therefore, the need for vigilance cannot be overemphasized.

STAFFING

Adequate staffing is critical in maintaining patient safety. There must be a minimum of 3 appropriately trained staff members present, which could include the proceduralist, the practitioner administering sedation (with the sole responsibility of monitoring the patient), and at least 1 additional staff member to provide assistance to the proceduralist and/or the practitioner providing sedation.

TRAINING FOR SEDATION BY NONANESTHESIA PRACTITIONERS

Training and responsibilities of health care workers providing procedural sedation is critical in maintaining patient safety. It is clear that the skills and abilities that must be acquired to safely provide deep sedation (eg, propofol sedation) are distinct from those required for minimal to moderate sedation (eg, conventional benzodiazepine/opioid sedation).
Important elements of a training program include the understanding of the pharmacology of the drugs used to provide sedation/analgesia and the ability to recognize the various levels of sedation. In addition, students should become proficient in the identification and management of potential complications, including advanced airway management techniques and cardiopulmonary resuscitation. Training should include both didactic and hands-on practical learning experience using life-size manikins and/or human simulators. In addition, proficiency should be acquired through preceptorship supervised by an anesthesiologist or a qualified clinician with privileges to administer deep sedation and/or general anesthesia. Certification in advanced cardiac life support alone clearly is not adequate. There should be regular retraining with emphasis on cardiovascular resuscitation, airway management, and exposure to new and updated clinical information.

The American Association for the Study of Liver Diseases, the American College of Gastroenterology, the American Gastroenterological Association Institute, and the American Society for Gastrointestinal Endoscopy collaborated recently to provide recommendations for NAAP for gastrointestinal endoscopy. The position statement states that nonanesthesiologists can safely administer propofol for gastrointestinal endoscopy provided they are properly trained and select patients wisely. This standpoint is in contradiction to the ASA statement that propofol should be used by practitioners trained in the administration of general anesthesia because of propofol’s narrow therapeutic range and lack of a reversal agent. The ASA recommends that the practitioners of moderate sedation should be able to rescue a patient transiting into deep sedation, while those practicing deep sedation should be able to rescue patients who inadvertently move into general anesthesia.

**DEVICES FOR SEDATION/ANALGESIA ADMINISTRATION**

One of the factors that might influence procedural sedation/analgesia in the future is the introduction of automated drug administration systems. Numerous sedation administration devices designed to achieve optimal procedural sedation/analgesia with improved patient safety have been investigated. These devices include patient-controlled sedation (PCS), target-controlled sedation, and computer-assisted personalized sedation (CAPS) systems.

PCS is a concept based on patient-controlled analgesia (PCA), which has become a standard of care for pain management. PCS attempts to address some of the limitations of current sedation/analgesia practices including variations in patients’ response to sedative-hypnotics, variations in patients’ expectations of the degree of sedation, and variations in requirements of sedation based on the level of stimulus. During PCS, patients can self-administer a sedative-hypnotic (e.g., propofol) to their desired needs. Patient satisfaction with PCS can be greater because of greater participation in the sedation process. Similar to PCA, there is an inherent safety in the PCS system, as patient feedback is necessary to administer a sedative-hypnotic. A PCS system would administer a predetermined dose of a sedative/hypnotic with a lockout period during which no drug will be administered. A recent study in patients undergoing colonoscopy reported that compared with PCS with midazolam and fentanyl, PCS with propofol and remifentanil provided rapid induction of sedation and early recovery.

Target-controlled infusion devices (TCI) are designed to achieve steady-state drug concentration based on pharmacokinetic-guided models. However, the TCI devices have some inherent limitations such as variations in pharmacokinetics. In contrast to these closed-loop systems, the newer automated anesthesia systems using
pharmacodynamic-guided models (eg, bispectral index-guided propofol administration) show promise. These devices appear to be superior to manual control devices, allow more rapid recovery, and improve quality of patient care. Of course, before such devices become the “standard of care,” the limitations of the pharmacodynamic variables (eg, bispectral index) used to guide drug administration will have to be addressed. In addition, the safety of these devices must be proven under varying clinical conditions. Further studies are needed to determine the optimal delivery system that would enhance patient safety.

A CAPS system (Sedasys; Ethicon Endo-Surgery, Inc, Cincinnati, OH, USA), comprising an automated propofol delivery device designed to provide minimal to moderate sedation, is currently seeking the approval of the FDA. This device integrates monitoring with pulse oximetry, capnography, electrocardiography, noninvasive blood pressure, and patient feedback to determine the dose of propofol. The Sedasys system responds to hypoxia and low respiratory rate or apneic episodes by encouraging the patient to breathe and/or stopping or slowing the propofol infusion, as well as increasing the flow rate of supplemental oxygen.

A recent study reported that compared with the midazolam/fentanyl technique, the Sedasys device precisely controlled propofol administration to achieve minimal to moderate sedation in patients undergoing gastrointestinal endoscopic procedures, and allowed early postprocedure recovery. However, this study can be criticized for several reasons. First, the dose of midazolam and fentanyl was higher than that used in routine practice. In addition, patients in the midazolam/fentanyl group received lower oxygen flow rate (2 L/min) compared with higher variable oxygen flow rate with the Sedasys device, which may have masked the incidence of hypoxia. Propofol boluses were required in 77% of procedures, suggesting a need for intervention as well as indicating the limitations of the alert system, as it can be overridden. The higher doses of midazolam/fentanyl in the “standard of care” group and the extra propofol boluses suggest the use of deeper levels of sedation in these patient groups.

The device is designed to provide a propofol infusion rate of less than 75 μg/kg/min with a 3-minute lockout between increases in maintenance dose, assuming that the patient responds appropriately to the periodic requests by the device. The health care provider using the device can administer additional propofol boluses of 25 μg/kg with a lockout interval of 90 seconds. This protocol allows for a maximum propofol dose of 200 μg/kg/min. Because the propofol dose for the maintenance of general anesthesia is 100 to 200 μg/kg/min, the Sedasys system may allow administration of general anesthesia by nonanesthesia practitioners, which may compromise patient safety. The device is equipped with red and yellow alerts, which indicate different levels of hypoxia and apnea. The device does not allow administration of propofol boluses during these alerts, which are specifically designed to prevent further propofol dosing.

In addition, in response to hypoventilation, the device increases the flow of fresh oxygen. As described earlier, supplemental oxygen in the setting of hypopnea or apnea can allow hypercarbia to go unnoticed for extended periods of time and delay intervention. The device will also encourage the subject to increase ventilation when inadequate ventilation is assessed either by respiratory rate or end-tidal CO₂. As mentioned previously, capnography allows for an accurate assessment of ventilation quality and can detect impending hypoxemia earlier than pulse oximetry.

It is recommended that this device be used only in patients younger than 70 years, in the presence of a 3-person clinical team whereby one person will have the sole responsibility of monitoring the patient, the device, and managing the patient’s airway.
This dedicated person must have advanced training and at least the skills of a nurse. Physicians using the device must complete a stringent educational program as well as demonstrate continuing competency (see earlier discussion). Finally, there is a need for further research to assess the appropriate use and safety of this device in older and sicker patients with comorbidities.

SUMMARY

The advantages conferred by the sedation and analgesia techniques have increased their popularity. The goal of sedation must be to minimize risk while maintaining an acceptable level of patient and practitioner satisfaction. In achieving adequate patient comfort, it is important to avoid compromising patient safety. Because the differences between the levels of sedation may be subtle and patients frequently move to a deeper level than originally intended (which can result in significant morbidity and mortality), the degree of care provided should be the same for all patients receiving sedation. Of importance is that the risks of deep sedation may even exceed those of general anesthesia in which the airway is already secured. Therefore, it is necessary to develop protocols for instituting training programs, patient selection and preparation, monitoring, sedation/analgesia techniques, and postprocedure recovery and discharge, as well as diagnosis and treatment of potential complications. Finally, anesthesiologists can play an important role in development of protocols, training programs, and quality assurance programs.

REFERENCES


