Propofol Infusion Platforms: Opportunities and Challenges

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Key Words

Patient-controlled infusion system • Target-controlled infusion system • Propofol

Abstract

Several propofol infusion platforms have been devised to address the inherent safety problems associated with propofol administration. Patient-controlled and target-controlled infusion systems have been described in the literature, and the Sedasys™ closed-loop feedback system is in FDA review. No matter what the infusion platform, there are important safety concerns that should be addressed whenever propofol is administered by non-anesthesiologists. There must be safeguards in the facility's sedation protocol for non-anesthesiologists that involve training, documentation, auditing/oversight, quality improvement and involvement of the facility's pharmacy and therapeutics committee. Definitions of levels of sedation and recommendations from the American Society of Anesthesiologists on rescue, identification and management of potential complications, as well as monitoring and training of personnel are also presented.

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Introduction

Propofol is a sedative with impressive properties including quick onset, quick offset and high-quality recovery. However, propofol is also a difficult sedative to achieve the level of sedation intended, due to intrinsic drug properties. Propofol is only a hypnotic and has no analgesic effect. Adding narcotics to propofol yields intense synergistic sedation effects. There is large interpatient variability, so careful dose titration is needed for every patient based on frequent assessments of their level of consciousness. Disinhibition makes 'conscious' sedation very difficult, contributing to the use of higher doses and deeper levels of sedation, possibly close to general anesthesia. When patients are deeply sedated, they are candidates for developing airway obstruction and loss of central respiratory drive. Hypersalivation occurs in 12% of cases with risk of laryngospasm and the need for emergent intubation. Propofol is a cardiac depressant and vasodilator, which becomes problematic in the bowel-prepped, NPO patient especially with coexisting cardiac disease. Furthermore, onset time can be delayed by minutes in the elderly, further complicating ease of titration.

There is a warning in the FDA-approved package insert for propofol. It states, 'For general anesthesia or monitored anesthesia care sedation, propofol should be ad-

ministered only by persons trained in the administration of general anesthesia and not involved in the conduct of the surgical/diagnostic procedure.' It is instructive to clearly define monitored anesthesia care [1]. According to the American Society of Anesthesiologists (ASA), monitored anesthesia care is delivered only by an anesthesia provider and is defined as monitoring multiple physiological parameters and anticipating the need to progress to general anesthesia. In addition, there is a possibility that the surgical procedure may become more extensive than originally thought and/or result in unforeseen complications. This is a very different situation than a patient under sedation/analgesia by a non-anesthesia provider in a gastroenterology suite.

In some practices, anesthesiologists have become involved in the administration of propofol for gastroenterology procedures. The gastroenterologist can then concentrate on the needed procedure, leaving monitoring, management and recovery to the anesthesia professional and thereby improving practice efficiency. However, there are added costs. One of the driving forces behind the question of whether anesthesiologists should be involved in gastroenterology procedures was put forward by the Aetna Insurance Company in the USA in 2007. At that time Aetna decided that they would not reimburse anesthesia for gastrointestinal procedures on patients with 'no sedation-related risk factors'. It appeared then that they would reimburse anesthesia only if patients were pregnant, age <18 or >65 years, had a high ASA status, had airway risk (morbidly obese, otolaryngological problems), were difficult to sedate, drug or alcohol dependent, required complex or long gastrointestinal procedures, or had epilepsy. In 2008, Aetna agreed to delay the effective date until 'more patient friendly alternatives' were developed for gastrointestinal procedures. This was generally assumed to be the expected advent of fospropofol and Sedasys™.

Propofol Infusion Platforms

Several propofol infusion platforms have been devised to address the inherent safety problems associated with propofol administration. Patient-controlled and target-controlled infusion systems have been well described in the literature [2–4]. More recently, Mandel et al. [5] published a study using patient-controlled sedation for colonoscopy, comparing propofol-remifentanyl versus midazolam-fentanyl. The propofol-remifentanyl patient-controlled sedation patients recovered significantly more

rapidly with higher patient satisfaction ratings, although they had lower provider safety ratings.

Recently, Ethicon Endo-Surgery developed a propofol sedation delivery system (Sedasys™). It is now in FDA trials and its intent is to deliver minimal-moderate sedation, not deep sedation, according to the ASA definitions. The system monitors HR, BP, SpO₂, and RR via end-tidal CO₂, and uses closed-loop feedback with an automated response monitor [6]. Thus, the patient should be able to respond purposefully to verbal commands, require no airway intervention and sustain adequate spontaneous ventilation, allowing individualized titration of dose to effect. However, Sedasys™ permits a care provider to override these safeguards and administer a bolus when the patient has triggered cautionary alarms.

Pambianco et al. [7] have published the only peer-reviewed report of Sedasys™. Forty-eight GI patients (24 from one center in Belgium and 24 from one in the USA) were studied, with an equal number colonoscopies and esophagogastroduodenoscopies at each center. The MOAA/S score was 2 or greater 99% of the time and 54% of patients had 'much or complete' recall, which is consistent with achieving moderate sedation. The procedure times were very short: 9.5–12 min for colonoscopies and 2.5–2.75 min for endoscopies. The propofol dosages were 83–103 and 42–50 mg, respectively. Recovery (as defined) occurred in seconds because of the short procedures and low doses. Safety was good, with no need for airway support; 6% desaturated <90% for >15 s and 38% had apnea >30 s. However, the media have reported patient deaths after propofol given by non-anesthesiologists. The initial use of midazolam is a cautionary reminder. When it was introduced in the USA in the late 1980s, there were 1,600 adverse reactions and 86 deaths associated with the drug in the first 5 years [8]. Nearly all of these were associated with sedation during endoscopy.

Important Safety Concerns when Using Propofol

No matter what the infusion platform, there are important safety concerns that should be addressed whenever propofol is administered by non-anesthesiologists. The ASA has an excellent statement that was first published in 2004 on the safe use of propofol [9]. This document states that because sedation is a continuum, a patient receiving propofol must receive the care required for deep sedation. It also defines the components of rescue from a deeper-than-intended level of sedation and the necessity to identify and manage associated airway and car-

diovascular complications. The document outlines the needed monitoring equipment and training of personnel, and is one of the few ASA statements that is jointly sponsored by the American Association of Nurse Anesthetists.

There must be important safeguards in any facility sedation protocol for non-anesthesiologists. These should involve training, documentation, auditing/oversight, quality improvement and involvement of the facility's pharmacy and therapeutics committee.

Training of the gastroenterologists and nurses involved in sedation must concentrate heavily on the pharmacokinetics and pharmacodynamics of the drugs used. No continuous infusion drips/pumps should be used. All personnel should be able to demonstrate their ability to rescue a patient who slips into the next level of sedation. Furthermore, an intensive, hands-on airway course is advised as well as advanced cardiac life support. The nurse assistants need to be trained in proper documentation, including the patient's SpO₂, respiratory rate, level of responsiveness and any airway intervention, such as a chin lift, jaw thrust, nasal or oral airway, positive pressure ventilation by mask, and any use of a laryngeal mask airway or endotracheal tube.

Audit and oversight are important program components. The facility should routinely certify and review the sedation site leadership for both nurses and physicians.

Continuous quality improvement indicators must be collected and evaluated. Random chart review is important as well as unannounced observation by the facility's quality management officers. Regular morbidity and mortality conferences directed at difficult cases are important to improve quality and should involve both nurses and physicians.

The involvement of a facility's pharmacy and therapeutics committee is important to control the use of drugs employed in sedation to approved locations and personnel. This oversight helps ongoing review of drugs employed as well as new drugs that become available. There should be an anesthesiology representative on the committee.

Conclusions

In summary, there are new platforms for the use of propofol, but one must recognize that this drug has a very narrow therapeutic window with the potential for serious side effects, no matter by whom or how the drug is administered. There may be other new drugs on the horizon that might be better, but again, this always needs to be looked at with an eye towards improving patient safety.

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