

PRACTICAL CONSIDERATIONS IN SEDATION MANAGEMENT TO IMPROVE OUTCOMES

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Maintaining an accurate level of sedation for the patient in the intensive care unit (ICU) is important because too much or too little sedation can result in deleterious consequences. To help achieve optimal sedation, clinicians must consider the various means available today to measure sedation levels, the selection of sedative agents that may produce improved outcomes, and the benefits of implementing sedation protocols.

Sedation Scales: Beyond the Ramsay Scale

In discussing sedation scales, David B. Glick, MD, from the University of Chicago Medical Center in Illinois said, “We first need to ask: Why do we even need a scale at all?”

Sedation scales serve a number of important purposes. They communicate information between members of the service team, across different teams, and beyond to clinicians worldwide through the literature. These scales also provide sedation targets, permitting the patient’s needs to be matched with the drugs and techniques in use. As another important benefit, sedation scales facilitate the use of protocols and also provide information to enable the comparison of drug efficacies.

“All these points make it clear that to effectively titrate sedative agents to appropriate levels, we need a reliable scale for measuring the effectiveness of the sedation,” Glick said.

Patients who receive too little sedation may cause harm to themselves by pulling out lines or falling out of bed. Undersedated patients are at risk for harming others through flailing or other actions, and their “awareness” could be disturbing, leading to post-traumatic stress disorder-like effects. In addition, the potential for stress-related cardiovascular effects, such as tachycardia and hypertension, could induce a cardiac event. Inadequately sedated ICU patients also are at risk for ventilator dyssynchrony.

“There also are risks associated with having too much sedation, beginning with difficulty to extubate and, as a result, prolonged intubation,” added Glick. This may lead to longer ICU and hospital lengths of stay. In addition, oversedation is associated with increased use of procedures (e.g., head scans, placement of parenteral feeding lines, tracheostomy) that might be unnecessary with appropriate sedation, as well as with increased risk of reintubation for extubated patients. “In addition to these known risks, long-term cognitive dysfunction and increased mortality rates have been reported with prolonged general anesthesia during surgery (Monk et al. *Anesth Analg*. 2005;100:4), and the same may hold true for patients in the ICU,” added Glick.

The Ramsay scale, developed about 30 years ago, is still the most widely used scale for evaluating levels of sedation in recovery rooms and many ICUs. The scale is numbered from 1 to 6, with 1 signifying the most anxious or agitated state and 6 indicating an unresponsive state, even to fairly vigorous stimuli.

“I think the Ramsay scale remains the most widely used sedation scale because it’s simple to use, familiar to staff and reliable,” said Glick. “But there are significant limitations in using it in the ICU,” he continued. “First and foremost, the Ramsay scale has only one level that covers all forms of agitation; the other five levels refer to varying levels of sedation.”

Glick discussed other problems associated with the Ramsay scale. Because only one of the six levels addresses agitation, the levels on the scale are not evenly distributed, rendering it impossible to obtain a meaningful average for multiple readings from one patient and making it difficult to analyze the data statistically. Furthermore, the scale’s various levels are not mutually exclusive, thwarting the ability to obtain an accurate reading. It also fails to provide a target level for sedation.

“Such concerns have prompted efforts to characterize and find an optimal sedation scale,” Glick said. See Table 1 for attributes of the ideal sedation scale.

Interest in an optimal sedation scale has led to the emergence of the following strategies for identifying sedation levels:

- **Harris Scale.** Described in 1991 by Harris and colleagues, this scale is designed for use in patients receiving mechanical ventilation.
- **Comfort Scale.** This scale, developed in 1992, evaluates the levels of agitation levels in children.
- **Sedation Agitation Scale (SAS).** Riker and colleagues described the SAS in 1994. Ranging from 1 to 7, the scale contains three clearly defined levels for agitation, sedation and midpoints between agitation and sedation, with examples provided for every level. The target level for most patients is level 4 (calm/cooperative), although in some patients and situations, level 5 (agitated) or level 3 (sedated) might be appropriate.
- **Motor Activity Assessment Scale (MAAS).** Published by Devlin, the MAAS ranges from 0 to 6. It indicates specific responses to physical stimuli as well as to verbal command for each level.
- **Richmond Agitation-Sedation Scale (RASS).** The RASS, presented by Sessler and coworkers in 2001, contains 10 levels, with 0 (alert and calm) in the center, four levels above 0, and five levels below 0. Details regarding movement and other signs are provided for each level.

Because all these scales rely on the patient’s responsiveness, a problem emerges when both sedating and neuromuscular blocking agents are administered. “The evaluation of a patient who is receiving neuromuscular blocking agents would yield meaningless results on any of the scales defined to this point,” Glick explained.

“These new scales appear to meet the criteria of the optimal sedation scale, except in the area of validation,” said Glick. “Against what can you determine the value and validity of any of these scales? What is the gold standard?” Classically, a patient’s sedation level was evaluated using a visual analog scale in which the practitioner selects a point along a 0 to 10 scale to define the sedation level. Validation also might be accomplished by obtaining the expert opinion of intensivists or psychiatrists, by comparing the result with other scales (even though they themselves cannot be validated), or by simply “knowing that it seems right,” according to Glick.

“However, determining a patient’s level of sedation because ‘it feels right’ is inadequate,” he continued, “because it doesn’t allow any of the work we need to do to provide for efficacy evaluation of drugs or protocol implementation. It’s simply one person’s opinion.” He added that some hope electroencephalography (EEG) monitoring could emerge as a useful tool for measuring sedation levels, but it has not been shown to be effective yet.

In closing, Glick emphasized that a broadly accepted standard for evaluating sedation is essential to evaluate drug efficacies and manage sedation protocols. “There are many reliable and likely responsive scales available, but validation is problematic because no standard exists,” he said. “Wide adoption of any of the current scales probably would forward our goals to better gauge efficacy and enact protocols in the ICU. Perhaps improved neuromonitoring techniques will provide the as-yet elusive gold standard for determining a patient’s level of sedation.”

Table 1. Attributes of an Ideal Sedation Scale

- Reflects the presence and severity of the clinical condition(s), leading to sedative needs
- Offers defined optimal level of sedation
- Defines clearly discrete criteria for non-overlapping levels
- Identifies a sufficient number of levels to allow drug titration
- Demonstrates reliability and is easy to learn and implement
- Can be validated
- Responds to changes in sedation level over time

Selection of Sedatives that Improve Outcomes

“We all know there are a large number of sedative agents available for use in the ICU, but which of those is most likely to improve outcomes?” asked Timothy D. Girard, MD, MSCI, from Vanderbilt University School of Medicine in Nashville, Tennessee. He presented scientific evidence related to three sedative medications: propofol, remifentanyl, and dexmedetomidine. “All of these have been compared with the benzodiazepines, which are the most commonly used class of sedative agents,” he said.

In addition to reiterating the benefits of appropriate sedation that Glick previously discussed, Girard briefly addressed the complications associated with sedatives, including prolonged duration of mechanical ventilation, delirium, coma, and adverse psychological outcomes (Girard et al. *Lancet*. 2008;371:126). He cited data showing that, among patients receiving mechanical ventilation, use of lorazepam as well as other sedatives is associated with delirium (Pandharipande et al. *Anesthesiology*. 2006;104:21).

Propofol. “One possible choice of sedative to improve outcomes among ICU patients is propofol,” said Girard. Propofol is a short-acting sedative medication generally administered through continuous infusion, although in some circumstances it is given as a bolus. Like the benzodiazepine agents, propofol exerts its sedating effect through gamma-aminobutyric acid (GABA) agonism.

In one randomized controlled trial, continuous infusion of propofol was compared with intermittent bolus administration of lorazepam in medical ICU patients who received mechanical ventilation (Carson et al. *Crit Care Med*. 2006;34:1326). The most common diagnoses of these patients upon ICU admission were sepsis and acute respiratory distress syndrome (ARDS). The study found that duration of mechanical ventilation was reduced significantly with propofol versus lorazepam. Additionally, among survivors, ICU length of stay was lower in the propofol group compared with the lorazepam group. Hospital mortality was no different between groups.

“The authors concluded that because propofol is a short-acting sedative, patients were able to wake up more quickly when their respiratory failure improved to the point that they were ready to be extubated, and this led to superior outcomes,” Girard stated.

Remifentanyl. “An alternative sedative medication is remifentanyl, which also is short-acting,” said Girard. Acting as a mu-opioid agonist, remifentanyl has both analgesic and sedative properties. However, unlike benzodiazepine agents, remifentanyl typically does not cause amnesia.

In a study involving medical and surgical ICU patients who were ventilated and sedated, Breen and colleagues compared the use of a remifentanyl-based sedation strategy (titrated to a higher dose and/or a midazolam-based strategy as needed) with the most commonly used sedative agents in 15 European medical centers (Breen et al. *Crit Care*. 2005;9:R200). Patients in the control group who were receiving midazolam could be treated additionally with analgesics, including morphine or fentanyl, if necessary.

Results showed that patients in the remifentanyl group were weaned off the ventilator significantly earlier than patients in the midazolam-based group (see Figure 1). No significant differences in length of stay or mortality rates were observed.

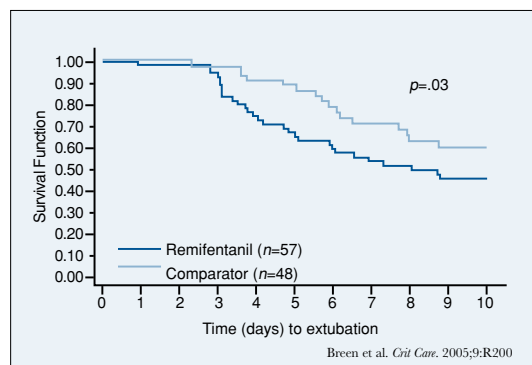


Figure 1. Time to Extubation Using Remifentanyl Versus Midazolam for Sedation.

Dexmedetomidine. “Unlike propofol and remifentanyl, the effect of dexmedetomidine on clinical outcomes has been evaluated in a double-blinded investigation,” explained Girard. Dexmedetomidine is an alpha 2-adrenoceptor agonist. It differs from agents that target the GABA receptors (e.g., benzodiazepine agents, propofol) and those that target opioid receptors (e.g., remifentanyl, fentanyl, morphine).

Although dexmedetomidine does not currently have an indication for the treatment of delirium approved by the Food and Drug Administration, its efficacy in delirium was evaluated in the randomized, double-blind clinical trial known as the Maximizing Efficacy of Targeted Sedation and Reducing Neurological Dysfunction (MENDS) study (Pandharipande et al. *JAMA*. 2007;298:2644). The objective of the study was to determine whether dexmedetomidine in comparison with lorazepam reduces the duration of delirium and coma in mechanically ventilated ICU patients while providing adequate sedation. The two primary outcomes were delirium- and coma-free days and efficacy of sedation. Medical and surgical ICU patients received continuous infusions of either dexmedetomidine or lorazepam. Both drugs could be titrated, and fentanyl could be added to either regimen as needed. Sepsis and ARDS were the most common diagnoses of the patients.

Results showed that accurate sedation was more likely among patients receiving dexmedetomidine compared with those receiving lorazepam (see Figure 2). “Oversedation was less likely to occur with dexmedetomidine than lorazepam,” said Girard. “Alternatively, the dexmedetomidine group had more occurrences of undersedation than the lorazepam group.”

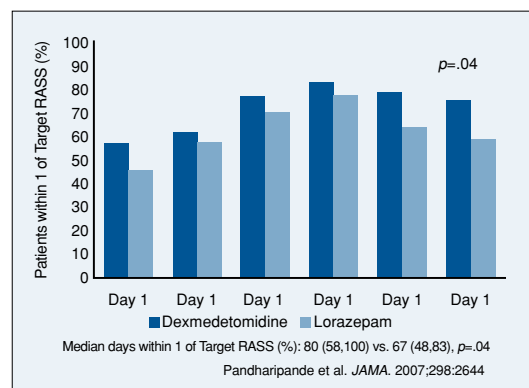
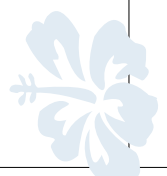


Figure 2. Patients Accurately Sedated Using Dexmedetomidine Versus Lorazepam.

In terms of brain dysfunction or the composite outcome of delirium- and coma-free days, the dexmedetomidine group had a median 7 days during the 12-day study period in which patients had normal neurologic status compared with a median 3 days for those in the lorazepam group. Ventilator-free days, ICU length of stay, and mortality rates did not differ statistically between the groups.

“Based on these studies, we can see we have work ahead of us before we know the most appropriate and optimal sedative medication,” concluded Girard. “Obviously, different medications will be selected for different patients, but the evidence currently shows that benzodiazepine agents appear to be inferior to at least the three medications discussed here: propofol, remifentanyl and dexmedetomidine.” More research is needed on this topic. The Society of Critical Care Medicine continues to investigate best practices and will release a revised sedation and analgesia guidelines in 2009.



The Benefits of Using Sedation Protocols

“When addressing sedation protocols, it’s important to keep in mind that if we don’t read the effects of analgesia well, pain will be poorly controlled and that will bring us to oversedation,” said Sergio D. Bergese, MD, from The Ohio State University in Columbus.

As noted by Glick and Girard, sedation and analgesia fulfill several purposes in acute care settings. In addition to providing adequate pain control, analgesia and sedation optimize the safety of patients and caregivers, enhance patient comfort, and facilitate mechanical ventilation. They also have been found to reduce anxiety, prevent delirium, induce sleep when required, and induce the appropriate level of amnesia (Ely et al. *JAMA*. 2003;289:2983; Blanchard. *Postgrad Med*. 2002;111:59; Kress et al. *Am J Respir Crit Care Med*. 2002;166:1024).

Providing the optimal level of sedation is essential to avoid the harmful ramifications of under- or oversedation. The goals of sedation and analgesia begin with optimizing the safety of patients and caregivers, relieving pain and anxiety, and attenuating the associated harmful adrenergic response. Other goals include improving patient compliance with care, facilitating communication with caregivers and family members, and avoiding or reducing delirium.

Clinicians can turn to various guidelines and standards to help them decrease the incidence of inadequate sedation.

The Joint Commission Standards. According to The Joint Commission standards, qualified personnel must be available to administer, monitor and evaluate patients who have received sedation. Institutions must define standards and assessment tools in their policies. In addition, documentation must be available in the patient’s medical record.

“One of the most important aspects of these guidelines was the emphasis on a multidisciplinary approach to sedation,” remarked Bergese. “Also, these institution-wide standards stressed the need to incorporate sedation guidelines at the bedside.”

Clinical Practice Guidelines for the Sustained Use of Sedatives and Analgesics in the Critically Ill Adult. Offering evidence-based recommendations for critically ill patients, these guidelines from the American College of Critical Care Medicine (ACCM) provide a systematic, multiprofessional approach to producing clinical and economic benefits. Pharmacologic agent and dose selections are based on sedation and analgesic goals. The potential for opioid, benzodiazepine and propofol withdrawal should be considered. For the agitated ICU patient, sedation should be provided only after giving adequate analgesia and treating reversible physiologic causes. A sedation goal needs to be established for each patient, and assessment and response to therapy should be documented using standard scales.

The ACCM guidelines also highlight the need to address sleep deprivation because of its association with impaired tissue repair, decreased cellular immune function, and induction of stress in ICU patients. Recommendations for sleep promotion include optimizing the environment and using appropriate pharmacologic therapy (Jacobi et al. *Crit Care Med*. 2002;30:119).

Bergese went on to discuss cooperative sedation, which provides several benefits and underscores the importance of avoiding oversedation. “In cooperative sedation, patients easily transition from sleep to wakefulness and task performance when aroused,” he explained. “Furthermore, they are able to resume rest when not stimulated.” Cooperative sedation is most useful during procedures in which communication with the patient must be maintained. It facilitates participation in therapeutic maneuvers and allows

for patient interaction in care decisions (Bekker et al. *Neurosurgery*. 2005;57(suppl 1):1; Burns et al. *Drugs*. 1992;43:507).

In contrast, poor cooperative sedation is associated with negative outcomes. “Pain that is not communicated in acute care settings can result in an increased stress response and a guarding of muscles and muscle rigidity around the area of pain, leading to pulmonary dysfunction, exhaustion and disorientation,” Bergese stated (Jacobi. *Crit Care Med*. 2002;30:119).

Bergese reviewed data describing the effects of implementing sedation guidelines within an institution. A prospective analysis of ICU patients who required mechanical ventilation and continuous analgesia, sedation, and/or neuromuscular blockade, showed length of hospital and ICU stay, as well as duration of mechanical ventilation, were shorter for patients in the guidelines group versus those treated before the guidelines were developed. Implementation of guidelines also led to a decline in mean drug costs across all drug classes studied (Mascia et al. *Crit Care Med*. 2000;28:2300).

Another study analyzed the clinical and cost outcomes associated with evidence-based clinical pathways and protocols for weaning acute care patients from mechanical ventilation (Burns et al. *Crit Care Med*. 2003;31:2752). In comparison to historic controls, patients who were treated according to the clinical pathway/protocol had significant reductions in ventilator days, ICU and hospital lengths of stay, and mortality rates. In addition, a cost savings of more than \$3 million was realized for the pathway/protocol group.

Positive outcomes from sedation protocols relating to pharmacy services, nursing, and other specialties also have been reported. Marshall et al studied the impact of a clinical pharmacist-enforced ICU sedation protocol on the duration of mechanical ventilation and hospital length of stay, noting that the protocol improved adherence to the sedation guideline and resulted in a significant decrease in the duration of mechanical ventilation (Marshall et al. *Crit Care Med*. 2008;36:427).

“Another study examined outcomes relating to a sedation protocol used by ICU nurses,” said Bergese. “The protocol allowed nurses to rapidly implement changes in pharmacotherapy without consulting a physician or pharmacist.” The results showed decreased rates of ventilator-acquired pneumonia sedation and decreased duration of mechanical ventilation among the protocol group, compared with the control group (Donnelly et al. *Am J Nurs*. 2004;104:72EE).

“It is important to note that a well-designed ICU protocol does not constrain decision making,” said Bergese. “Protocol-driven care does not eliminate the need for clinical judgment. Rather, continual appraisal from new data can be used to modify protocols and adjust new strategies.”

In concluding his discussion, he emphasized: “A multiprofessional, multifaceted approach to developing ICU sedation protocols is the answer. Such an approach appears to be critical for the success of ICU sedation.”

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Continuing Education Self-Assessment

PRACTICAL CONSIDERATIONS IN SEDATION MANAGEMENT TO IMPROVE OUTCOMES

- Which of the following criteria for the ideal sedation scale is not met by any of the scales available today?
 - Ability to validate the results
 - Responsiveness to changes over time
 - Sufficient number of levels to allow drug titration
- In a comparison with lorazepam, which of the following sedative agents has been shown to reduce the incidence of delirium among mechanically ventilated ICU patients?
 - Dexmedetomidine
 - Propofol
 - Remifentanyl

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