CURRENT ISSUES IN AGITATION MANAGEMENT

I. Larry Cohen, MD, FCCP, FCCM

ABSTRACT

Managing the agitated patient is an important aspect of treating the critically ill. While no comprehensive definition of agitation exists, it is generally understood that it includes both physical and emotional distress. This article describes the common signs of agitation, its major causes, and practical courses of treatment. Several levels of sedation can be achieved through proper medication and monitoring. Selecting the appropriate medication, continuing close monitoring throughout the sedation period, and conducting a thorough follow-up will greatly improve the patient's chances for a better long-term outcome.

ADVANCED STUDIES IN MEDICINE 2002;2(9):332-337

A fundamental tenet of caring for the critically ill patient is relief of suffering; maintenance of an optimal level of comfort has long been a universal goal of practitioners. Theories of management for the critically ill have changed considerably over the last decade and are expected to evolve even more drastically in the years to come as the evidence base for practice matures. In the early 1980s, eg, the goal of 67% of intensive care units (ICUs) was deep sedation—a complete detachment of the patient from the environment. Today, the more common goal is maintenance of mild sedation with the patient lightly asleep, yet responsive to stimuli and able to recover rapidly following discontinuation of sedatives.

Management of the agitated patient clearly has become a major issue in critical care, with the growing volume of interest illustrated by a drastic rise in the number of journal articles on the subject over the past 3 decades. Simultaneously, sedation in the ICU has become a powerful economic issue as research measures its impact on overall costs, including length of time on mechanical ventilation and days spent in the ICU.

DEFINITIONS

While management of agitation is a critical issue, no clear and concise clinical definition of “agitation” exists. Simple dictionary descriptions of violent motion and strong or tumultuous emotion can encompass both the nonsedated paralyzed patient and the comatose patient with patient-ventilator asynchrony. Most important, it covers both physical and emotional distress—factors that contribute heavily to agitation in the ICU.

Levels of sedation have been defined as:

- Minimal sedation (anxiolysis): a drug-induced state during which patients respond normally to verbal commands, either alone or accompanied by light tactile stimulation.
• Moderate sedation/analgesia (conscious sedation): a drug-induced depression of consciousness during which patients respond purposefully to verbal commands, either alone or accompanied by light tactile stimulation.
• Deep sedation/analgesia: a drug-induced depression of consciousness during which patients cannot easily be aroused, but respond purposefully following repeated or painful stimulation.
• Anesthesia: a drug-induced loss of consciousness during which patients are not arousable, even by painful stimulation.

**Diagnosis of Agitation**

Agitation has been described as the “motor restlessness that accompanies anxiety.” Continual movement, often characterized by constant fidgeting, side-to-side movement, pulling at dressings and/or bed sheets, and attempts at self-extubation, is common, as is disorientation to place, time, and even name. In nonventilated patients, conversation may be largely unintelligible and include shouting, calling out, or moaning. Commands frequently are not understood or are misunderstood. An exaggerated sensation of pain may be present, even though the actual cause of the agitation may be the need to urinate or have a bowel movement.

Vital signs are frequently abnormal and may include extremely high blood pressure, elevated respiratory rate, increased heart rate, and a high metabolic rate that results in an increase in oxygen requirements and caloric demand if left unchecked. Table 1 summarizes common descriptors of agitation.

**Causes of Agitation**

Agitation frequently is a manifestation of an underlying disease or problem. While a single, definitive cause of agitation is rarely identified, patients should be evaluated for reversible conditions such as hypoxemia, pain, cerebral events, metabolic/electrolyte imbalance, sepsis, hepatic encephalopathy, or side effects from drug therapy. Other possible underlying causes of agitation include hypotension; hyper- and hypoglycemia; uremia; elevated levels of heavy metals such as lead, mercury, and manganese; brain injuries or thrombotic strokes; and nervous system abnormalities such as ischemia or malignancy. Alcohol, drug, or tobacco withdrawal may also contribute to agitation.

Finally, the ICU environment itself can be a cause of agitation. Sleep deprivation; constant bright lights; noise; being restrained and/or lying in one position; frustration with an inability to communicate or move; ventilator malfunction or significant patient-ventilator desynchronization; and intubation can all contribute to agitation.

Sedation of the agitated patient should be initiated only after reversible physiological causes have been treated. When used appropriately, sedatives reduce the risk of complications associated with the metabolic response to an injury and improve tolerance for invasive interventions, such as intubation, mechanical ventilation, tracheal suctioning, and dressing changes.

**Monitoring**

The ever-changing condition and requirements of sedated patients necessitate frequent assessment and

**Table 1. Signs and Symptoms of Agitation**

<table>
<thead>
<tr>
<th>Physical Signs</th>
<th>Vital Signs</th>
<th>Emotional/Mental Signs</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Restlessness</td>
<td>• Elevated blood pressure</td>
<td>• Disorientation</td>
</tr>
<tr>
<td>• Thrashing about in the bed</td>
<td>• Elevated respiratory rate</td>
<td>• Shouting, moaning, calling out</td>
</tr>
<tr>
<td>• Pulling at catheters, tubes, and restraints</td>
<td>• Increased heart rate</td>
<td>• Unintelligible conversation</td>
</tr>
<tr>
<td>• Overt breathing the ventilator</td>
<td>• Increased metabolic rate</td>
<td>• Inability to follow requests or commands</td>
</tr>
<tr>
<td>• A synchrony with ventilator settings</td>
<td>• Decreases in PO₂</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Increase or decrease in PCO₂</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Tachycardia</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Tachypnea</td>
<td></td>
</tr>
</tbody>
</table>
re-evaluation in order to ensure optimal patient management. A number of semiquantitative, subjective monitoring scales have been developed and examined for ICU use. An ideal scale should be easy to apply and have clear gradations between levels, thereby allowing for easier titration of interventions.4 As of yet, no system has been tested for its ability to detect a patient’s response to changes in therapy, dose, or withdrawal.8 While a true “gold standard” in scales does not exist, use of monitoring tools as a part of a protocol-driven intervention plan has been shown to improve patient outcomes regarding such issues as reduced time on mechanical ventilation and shortened length of ICU stay.4,8

The most commonly used and investigated tool is the Ramsay Sedation Scale, although it has been criticized for its lack of clear discrimination and specific descriptors that differentiate between levels of sedation.8 The Ramsay Scale provides 6 levels of sedation, including 3 levels of awake states and 3 levels of asleep states (Table 2).

Three subjective scales include:

• Riker Sedation-Agitation Scale (SAS): The first scale proven reliable and valid in the assessment of critically ill adults, it identifies 7 levels, ranging from dangerous agitation to deep sedation.

• Motor Activity Assessment Scale: Similar in structure to the SAS, it identifies 7 levels of agitation based upon patient behaviors, ranging from “unresponsive” to “dangerously agitated and uncooperative.”

• Confusion Assessment Method for ICU: This tool for assessing delirium has been tested in combination with a sedation scale or the Glasgow Coma Scale, and is currently undergoing validation. It is easy to apply at bedside, with interrater reliability, sensitivity, and specificity. The scale measures acute onset of mental status changes or fluctuating course, inattention, disorganized thinking, and altered level of consciousness. As opposed to the others listed above, it is more of a diagnostic tool than a true monitoring one.

The development of quantitative monitoring applications looks promising for the assessment and management of sleep and in the use of deep sedation, particularly when neuromuscular blockades are used.8 In current practice, objective scores are based on a patient’s electroencephalogram (EEG). The Bispectral Index (BIS) incorporates several EEG components in order to provide a discrete value ranging from 100 (completely awake) to <60 (deep sedation) and <40 (deep hypnotic state or barbiturate coma). While the BIS has been shown to be reliable in the operating room, it has not been thoroughly tested in the ICU.4,8 Bispectral Index scores may vary between different patients at the same subjective level of sedation, and other scales may be more reproducible.8 One study found that the BIS is an accurate predictor of response to verbal commands during sedation and hypnosis with propofol, with accuracy maintained when drug concentrations were increased or decreased.4 New BIS software is currently undergoing testing for applicability in measuring sedation in the ICU.8

**Systems Management: The Need for Standardization**

Once pain has been alleviated, the primary goals of sedation are anxiolysis, hypnosis, and amnesia; in some patients, respiratory depression and/or an antitussive effect are also desired.2 Current choices for sustained sedation include benzodiazepines and propofol in combi-
junction with opioids if analgesia is desired. The choice of a specific sedative depends on the patient's individual requirements, including duration of sedation, need for a rapid awakening, or presence of delirium. The patient's underlying condition and anticipated length of stay in the ICU are also considered.2,4

It is estimated that sedatives and analgesics account for 10% to 15% of total drug costs in medical and surgical ICUs.9 As a result, pharmacoconomics has become a key factor in sedative selection, with decisions based not solely upon acquisition cost, but on outcomes associated with sedation, such as shortened time on mechanical ventilation, shortened stay in the ICU, rapid awakening, and ease of titration. Consequently, the emerging standard of care is the use of standardized protocols and clinical practice guidelines to assist in the selection of the most appropriate sedative.6

Three studies found that protocol-driven sedation demonstrated significant reductions in duration of sedation, time on mechanical ventilation, length of stay in the ICU and hospital, and in drug costs.10-12 Brook et al conducted a randomized, controlled trial of patients in a medical ICU, and found that protocol-driven treatment resulted in less time on mechanical ventilation, shorter lengths of stay in the ICU and the hospital, and fewer tracheotomies.11 Devlin et al found that total sedation drug costs decreased from $4515 to $1152 post-guideline implementation (P = .081), while median patient sedation cost decreased from $11.27 (range $0-$1340) to $3.55 (range $0-$250). A high degree of guideline compliance was found to decrease sedation drug costs by 75%.10 Mascia et al found that total sedation costs were reduced from $4515 to $1152 following implementation of guidelines.12

Kress et al conducted a study of protocol-directed daily awakening of sedated patients. Daily interruption of infusion was found to shorten the duration of mechanical ventilation by more than 2 days and the length of stay in the ICU by 3.5 days, as well as to reduce the total dose of midazolam by nearly 50%.13 Nonetheless, the use of practice guidelines remains controversial across hospital disciplines. To be effective, development of guidelines requires multidisciplinary input with agreement among caregivers on monitoring scales and tools. Furthermore, it is essential that thought be given to the system as a whole, since numerous factors affect the final effect of any protocol.

The Figure illustrates the factors that can lead to agitation in critically ill patients. This cause-and-effect, or "fishbone," diagram should prove useful for performing root cause analysis and developing strategies for systems improvement in managing agitation in the ICU.

For any improvement strategy, such as protocols, to be successful, additional and ongoing training is required for all physicians, nurses, and other bedside caregivers. It is also important to track and communicate results in a simple, accurate, and timely manner.4

The American College of Critical Care Medicine first published practice parameters for the optimal use

![Image of Figure: Factors That May Impact Agitation in Critically Ill Patients](image-url)
of sedatives and analgesics in 1995; these guidelines recently have been updated and rereleased, and recommend a tiered approach that is based largely on expert opinion. The guidelines include recommendations on sedation assessment and therapy.

**Post-ICU Depression and Stress Syndromes**

Mental disorders, including anxiety, depression, and posttraumatic stress disorder (PTSD), can arise following traumatic and stressful events. Indeed, stress from an ICU stay can leave patients with psychological symptoms that can impair quality of life; depression and stress disorder symptoms have been found to last as long as 6 to 41 months following ICU treatment.

Schelling et al studied the incidence of PTSD in patients discharged from the ICU and found that 27.5% of patients suffered self-reported PTSD. Post-traumatic stress disorder scores were found to correlate to length of ICU stay (higher scores/longer stay). Scragg et al report that approximately 30% of discharged ICU patients experience post-traumatic stress symptoms, and about 15% meet the criteria for PTSD.

Emerging evidence indicates that symptoms of stress disorder and depression also are related to the use of sedatives. Further, stress disorder may be related to a patient’s memories of the ICU. Patients not receiving sedative therapy may recall an unpleasant or frightening ICU stay, leading to symptoms of PTSD. Conversely, patients who have clear, as opposed to delusional, memories of the ICU—even if those memories are unpleasant—appear to have a lesser risk for developing PTSD. As PTSD and depression can have a great influence on post-ICU quality of life, their full socioeconomic impact needs to be better understood. It is quite possible that drug choice in the ICU will ultimately be affected by this consideration.

**Selecting Pharmacological Agents**

The ideal sedative agent would have a rapid onset; provide adequate sedation; allow easy titration and rapid recovery following discontinuation; be easy to administer; lack drug accumulation; have minimal adverse effects; and be inexpensive. Unfortunately, no single drug has all of these characteristics.

When choosing a pharmacologic agent, the following issues should be considered: goal of individual patient therapy; duration of treatment; cause and type of agitation; mechanical versus nonmechanical ventilation; predictability of drug action; risk for secondary drug withdrawal and delirium; risk for post-ICU stress disorder or depression; immune compromise and antioxidant properties; need for rapid awakening; drug acquisition cost; and cost effectiveness. Drug selection is discussed on page 343.

**Conclusions**

Agitation is an important issue for those concerned about improving the quality, enhancing the outcome, and the practice of evidence-based critical care. Accurate diagnosis, diligent monitoring, and follow-up, as well as selection of an appropriate pharmacological therapy, are key to successful outcomes. Systemizing the approach to management of agitation through use of protocols, objective and semiquantitative measurements, and study of the post-ICU patient can lead to decreased lengths of stay, shortened duration of mechanical ventilation, decreased drug and care costs, and better long-term outcomes.

The topic of agitation is rapidly evolving for the critical care practitioner. It is quite conceivable that existing routine practices—especially in the area of sedative use—will become obsolete over the next 5 to 10 years. These changes will be driven by better scientific evidence, increasingly sophisticated regulatory guidelines, and, possibly, a more enlightened medicolegal community.

**References**


