PROTOCOLIZING AND MONITORING SEDATION, ANALGESIA AND DELIRIUM IN THE CRITICALLY ILL

Introduction

Critically ill patients are routinely mechanically ventilated, undergo repeated bedside procedures and are likely to have anxiety and pain. Thus, a variety of sedatives and analgesics are employed in the ICU to provide patient comfort, amnesia, reduce hemodynamic instability, and to blunt the stress response. Recent investigations have shown that continuous intravenous sedation is associated with prolonged mechanical ventilation and increased morbidity, and that daily interruption of sedation via a protocol of daily awakening trials improves patients’ outcomes dramatically.

Another area of concern associated with sedation, is the problem of delirium and long-term cognitive impairment. Recent studies have shown that delirium occurs in over 80% of mechanically ventilated patients and is a major independent determinant of length of stay, cost of care, and 6-month mortality.

Sedation selection in the ICU and goal directed therapy

Sedation and analgesia strategies in the ICU usually comprise of a combination of benzodiazepines and narcotics. A number of investigators have shown that nurse implemented sedation protocols in the ICU, as well as goal directed sedation resulted in shorter ventilator times, decreased length of stay and decreased ICU costs. Based on these, the Society of Critical Care Medicine (SCCM), recently published guidelines for the use of sedatives, analgesics and neuromuscular blockers in the critically ill.

SCCM recommendations

The SCCM guidelines offer evidence based drug recommendations depending on the duration of sedation and co-morbid conditions in critically ill. They too emphasize the need for protocolized sedation strategies as well as recommend goal directed therapy based on sedation scales.

- **Analgesia** - hemodynamically stable- morphine, otherwise fentanyl or hydromorphone
- **Anxiety**
  - Acute agitation- midazolam,
  - Short term sedation- midazolam or propofol
  - Long term sedation- lorazepam.
  - For patients with elevated intracranial pressures and compromised cerebral perfusion pressure, propofol is recommended with frequent reevaluation
- **Delirium**- haloperidol

The Vanderbilt Goal

- Use of a reliable validated scales to guide drug usage and evaluating patients for pain, anxiety and delirium- SCCM Grade A recommendation
- Development of standardized sedation protocol incorporating SCCM guidelines, with modification for local use
- IMPROVING PATIENT CARE

Monitoring analgesia

Patients in the ICU are evaluated for pain either by a Numerical Rating Scale (NRS) or by Behavioral & Physiological Indicators (BPI). Often we are utilizing the BPI since our patients are unable to communicate their pain due to their co-morbid conditions, sedation or mental status.
Monitoring sedation- The Richmond Agitation Sedation Scale (RASS)
There are to date 25 scales developed for assessing sedation. Only 3 have been validated in ICU patients. Of those validated the Ramsay Scale and the Riker –Agitation scale (SAS)/ Motor agitation Scale (MAAS) do not differentiate between verbal and motor stimulus. Additionally the SAS and MAAS are difficult to memorize since they don’t have precise discriminating factors. The Richmond Agitation Scale was developed in 1998 and validated at Medical College of Virginia by Curt Sessler, MD and a multidisciplinary team. It differentiates between motor and verbal stimulus and each category has very precise definitions, making it easy for communication of sedation goals between various care providers. Since the original validation study, it has been revalidated and shown to be a reliable instrument in a large cohort at Vanderbilt University.

Richmond Agitation Sedation Scale (RASS)

<table>
<thead>
<tr>
<th>Score</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>+4</td>
<td>Overtly combative, violent, immediate danger to staff</td>
</tr>
<tr>
<td>+3</td>
<td>Pulls or removes tube(s) or catheter(s); aggressive</td>
</tr>
<tr>
<td>+2</td>
<td>Frequent non-purposeful movement, fights ventilator</td>
</tr>
<tr>
<td>+1</td>
<td>Anxious but movements not aggressive vigorous</td>
</tr>
<tr>
<td>0</td>
<td><strong>Alert and calm</strong></td>
</tr>
<tr>
<td>-1</td>
<td>Not fully alert, but has sustained awakening (eye-opening and eye contact) to voice (≥10 seconds)</td>
</tr>
<tr>
<td>-2</td>
<td>Briefly awakens with eye contact to voice (&lt;10 seconds)</td>
</tr>
<tr>
<td>-3</td>
<td>Movement or eye opening to voice (but no eye contact)</td>
</tr>
<tr>
<td>-4</td>
<td>No response to voice, but movement or eye opening to physical stimulation</td>
</tr>
<tr>
<td>-5</td>
<td>No response to voice or physical stimulation</td>
</tr>
</tbody>
</table>

Procedure for RASS Assessment
1. Observe patient
   a. Patient is alert, restless, or agitated. (score 0 to +4)
2. If not alert, state patient’s name and say to open eyes and look at speaker.
   b. Patient awakens with sustained eye opening and eye contact. (score -1)
   c. Patient awakens with eye opening and eye contact, but not sustained. (score -2)
   d. Patient has any movement in response to voice but no eye contact. (score -3)
3. When no response to verbal stimulation, physically stimulate patient by shaking shoulder and/or rubbing sternum.
   e. Patient has any movement to physical stimulation. (score -4)
   f. Patient has no response to any stimulation. (score -5)

Monitoring delirium- The Confusion Assessment Method for the ICU (CAM-ICU)

Delirium
DSM IV criteria: a disturbance of consciousness with inattention accompanied by a change in cognition or perceptual disturbance that develops in a short period of time (hours to days) and fluctuates over time.
- Changes in cognition: memory impairment, disorientation and rambling or irrelevant speech.
- Perceptual changes: hallucinations (usually visual), illusions and delusions.

Delirium Subtypes
- Hyperactive delirium – seen in <1% of delirious patients - agitation, restlessness, pulling catheters or tubes, hitting, biting, and emotional lability. (At risk for self-extubation and subsequent reintubation)
- Hypoactive delirium –seen in about 35% of delirious patients, and associated with the worst prognosis-withdrawal, flat affect, apathy, lethargy and perhaps even unresponsiveness; often unrecognized due to these “quiet” symptoms; (At risk for aspiration, pulmonary embolism, decubitus ulcers, and other complications related to immobility)
- Mixed – combination- 64%
**Delirium in the ICU**

Until recently delirium was considered an unavoidable occurrence of ICU stay and no significant attempts had been made to quantify delirium and its implications in the critically ill. Recent work by Ely et al. using the Confusion Assessment Method for the Intensive Care Unit (CAM-ICU), has shown that delirium is extremely common in mechanically ventilated ICU patients and is associated with prolonged hospital stays, ongoing neuropsychological deficits, higher costs and increased mortality. Guidelines for the use of sedatives and analgesics in the critically ill adult from the SCCM have emphasized that the study of delirium and other forms of cognitive impairment in mechanically ventilated patients after ICU care may be an important advancement in the monitoring and treatment of critically ill patients.

**Confusion Assessment Method for the ICU (CAM-ICU)**

<table>
<thead>
<tr>
<th>I. Acute onset or fluctuating course</th>
<th>Absent</th>
<th>Present</th>
</tr>
</thead>
<tbody>
<tr>
<td>A. Is there evidence of an acute change in mental status from the baseline? OR B. Did the (abnormal) behavior fluctuate during the past 24 hours, that is, to come and go, or increase and decrease in severity as evidenced by fluctuation on a sedation scale (e.g. RASS), GCS, or previous delirium assessment?</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>II. Inattention</th>
<th>Absent</th>
<th>Present</th>
</tr>
</thead>
<tbody>
<tr>
<td>Did the patient have difficulty focusing attention as evidenced by <strong>scores less than 8</strong> on either the auditory or visual component of the <strong>Attention Screening Examination (ASE)</strong>?</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Auditory**
The rater explains to the patient that he or she will be reciting 10 letters with intermixed “A”s, and the patient should squeeze the rater's hand when he/she hears the letter ‘A’. The rater then recites slowly the following 10 letters-SAVE A HAART. Score 1 point for every appropriate response either a hand squeeze for the ‘A’ or no squeeze for the other letters. Usually the auditory test is all that is required to document inattention.

**Visual**
The patient is shown 5 simple pictures at 3-second intervals and asked to remember them. They are then immediately shown 10 subsequent pictures and asked to nod “yes” or “no” according to whether or not they have or have not just seen each of the pictures. Since 5 pictures have been shown to them already (correct nod = Yes), and five others are new (correct nod = No), patients are scored perfectly if they achieved 10 correct yes or no “nods.”

<table>
<thead>
<tr>
<th>III. Disorganized thinking</th>
<th>Absent</th>
<th>Present</th>
</tr>
</thead>
<tbody>
<tr>
<td>Is there evidence of disorganized or incoherent thinking as evidenced by <strong>incorrect answers to 3 or more of the 4 questions and/or inability to follow the commands</strong>?</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Questions**
1. Will a stone float on water?
2. Are there fish in the sea?
3. Does one pound weigh more than two pounds?
4. Can you use a hammer to pound a nail?

**Commands**
1. Are you having any unclear thinking? 2. Hold up this many fingers. (Examiner holds two fingers in front of patient) 3. Now do the same thing with the other hand. (Not repeating the number of fingers)

<table>
<thead>
<tr>
<th>IV. Altered Level of Consciousness</th>
<th>Absent</th>
<th>Present</th>
</tr>
</thead>
<tbody>
<tr>
<td>Is the patient’s level of consciousness anything other than <strong>alert</strong> such as vigilant, lethargic, or stupor? (e.g., RASS other than “0” at time of assessment) <strong>Alert</strong> spontaneously fully aware of environment and interacts appropriately <strong>Vigilant</strong> hyperalert <strong>Lethargic</strong> drowsy but easily aroused, unaware of some elements in the environment, or not spontaneously interacting appropriately with the interviewer; becomes fully aware and appropriately interactive when prodded minimally <strong>Stupor</strong> becomes incompletely aware when prodded strongly; can be aroused only by vigorous and repeated stimuli, and as soon as the stimulus ceases, stuporous subject lapse back into the unresponsive state</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Overall CAM-ICU (“YES” to Features 1 and 2 and either Feature 3 or 4):**

| Yes | No |
Figure 1- Flow Diagram of CAM-ICU (note: patients are delirious if they have Feature 1 and Feature 2, and either Feature 3 or Feature 4)

**Pharmacology of commonly used drugs**

**Anxiolytics and sedatives**

Lorazepam is a benzodiazepine of intermediate duration of action and may be administered as an infusion or by intermittent bolus injection. Like other benzodiazepines, it has anticonvulsant properties. Given its terminal elimination half-life (10-20 hr), it is the benzodiazepine of choice for prolonged sedation. It depends on glucuronidation and not the cytochrome p450 mechanism for metabolism in the liver, so is not significantly altered in hepatic insufficiency. It is still prudent to decrease lorazepam doses in the patient with liver disease. Another advantage is no change in elimination half-life in renal disease.

Midazolam is a short-acting, hydrophilic benzodiazepine that becomes a lipophilic compound in the blood. It is metabolized in the liver to α-hydroxymidazolam which has some sedative activity. Accumulation of the parent drug and its metabolite can produce a longer than expected duration, particularly in critical illness or hepatorenal dysfunction.

Propofol is an alkylphenol which is formulated in 10% Intralipid®. It is properly classified as an anesthetic, as it does not possess the ceiling effect of the above sedatives. Therefore, it is more appropriately used to sedate intubated, mechanically ventilated patients. In those patients who are ready to do so, it allows more rapid weaning from the mechanical ventilator than benzodiazepines due to its short duration of action and lack of accumulation. For the same reasons, of all currently used sedatives it can most easily be titrated to a desired level of consciousness. At anesthetic doses, it can cause hypotension secondary to vasodilation and, to a lesser degree, direct myocardial depression. Although a cerebral vasodilator, propofol reduces intracranial pressure and has anticonvulsant properties; it may provide cerebral protection in the head-injured patient providing hypotension is avoided. Its formulation in Intralipid® mandates that intravenous tubing be changed every day, that strict aseptic technique be adhered to in handling the drug, and that preferably a dedicated infusion port be utilized and that total parenteral nutrition be adjusted for lipid content.

Dexmedetomidine (Precedex) is a selective alpha-2 receptor agonist that has sedative, analgesic and anesthetic properties when given as a slow infusion. It undergoes rapid distribution, the distribution half life being only 6 minutes. It is indicated for short term sedation in the ICU. It has no respiratory depression and so can be used for hemodynamically unstable patients, or for patients who need sedation for a short period but cannot afford to have respiratory depression. A bolus of 1mcg/kg is given over 10 minutes followed by an infusion of 0.1-0.8 mcg/kg/hr. Rapid administration of the bolus can cause severe bradycardia, hypotension or hypertension.

**Analgesics**

Morphine is suitable when given by infusion or patient-controlled intravenous analgesia. It is particularly appropriate when administered by infusion over several days, because of its relatively low volume of distribution and rapid hepatic clearance. However, caution is exercised in the patient with renal insufficiency as its water-soluble metabolites (morphine 3- and 6-glucuronide) have analgesic efficacy and are dependent on renal elimination.

Fentanyl possesses one-hundred times the potency of morphine, but has similar efficacy. Because of its
high lipophilicity, it is rapidly acting and widely distributed. It has high accumulative potential secondary to both its high volume of distribution and slow hepatic clearance. As a result, its half-life increases progressively from 30 minutes to 9-16 hrs with continuous infusion, and care must be taken to adjust infusion rate with time. Fentanyl is suitable for patients with morphine allergy and established renal insufficiency. Unlike morphine, it does not cause histamine release and is purported to afford greater hemodynamic stability as a result. However, all sedatives and analgesics cause hypotension usually by sympatholysis, and must be used with caution in those patients with hypovolemia, cardiac failure and cardiac tamponade.

ANTIDELERIUM DRUGS

Haloperidol is a useful drug for the treatment of delirium. It is particularly safe in non-intubated patients because it rarely causes respiratory depression. It may cause exacerbation of parkinsonism and should be used with caution when combined with other centrally acting antidopaminergics, including metoclopramide. Haloperidol causes QT prolongation, which may be exacerbated in the presence of class III antiarrhythmics, hypocalcemia and intracranial hypertension. It is a mild α-adrenergic antagonist. Its safety has been questioned in acute head injury, as animal studies suggest worsening of secondary brain injury by the central antidopaminergic effect.

References


