Assessing and Managing Sedation

William R. Beam, MD, FCCP
Medical Director of Critical Care Services
Medical Director, Sleep Disorders Center
Program Director, Sleep Medicine Fellowship
St. Mary's Hospital
St. Mary's Medical Center
Clinical Assistant Professor in Medicine
Marshall University School of Medicine
Huntington, West Virginia

Faculty Disclosure

It is the policy of The France Foundation to ensure balance, independence, objectivity, and scientific rigor in all its sponsored educational activities. All faculty, activity planners, content reviewers, and staff participating in this activity will disclose to the participants any significant financial interest or other relationship with manufacturer(s) of any commercial product(s)/device(s) and/or provider(s) of commercial services included in this educational activity. The intent of this disclosure is not to prevent a person with a relevant financial or other relationship from participating in the activity, but rather to provide participants with information on which they can base their own judgments. The France Foundation has identified and resolved any and all conflicts of interest prior to the release of this activity.

William R. Beam, MD, FCCP, has nothing to disclose.
Assessing and Managing Sedation

Learning Objectives

• Describe current guidelines for the management of pain, agitation, and delirium in adult patients in the intensive care unit
• Use validated scales to measure sedation, pain, agitation, and delirium in critically ill patients
• Compare the benefits and limitations of available sedatives and analgesics in the acute care, procedural, and surgical settings

Goals for Sedation and Analgesia

• Prevent pain and anxiety
• Decrease oxygen consumption
• Decrease the stress response
• Patient-ventilator synchrony
• Avoid adverse neurocognitive sequela
  – Depression
  – PTSD
  – Dementia
  – Anxiety


Assessing Pain: FACES Scale 0–10


Other Scales
• Behavioral Pain Scale (BPS) 3-12
• Critical Care Pain Observation Tool 0-9
Managing Pain in the ICU: Opioids

**Clinical Effects**
- Analgesia
- Sedation

**Adverse Effects**
- Respiratory depression
- Hypotension
- Bradycardia
- Constipation
- Tolerance
- Withdrawal symptoms
- Hormonal changes

---

**What Is the ABCDE Bundle?**

*We Need Coordinated Care*

- Many tasks and demands on critical care staff
- Great need to align and support the people, processes, and technology already in ICUs
- ABCDE bundle is multicomponent, interdependent, and designed to:
  - Improve clinical team collaboration
  - Standardize care processes
  - Break the cycle of oversedation and prolonged ventilation

---

**What Is the ABCDE Bundle?**

- Awakening and Breathing Trial coordination
- Coordination/Choice of Sedation
- Delirium Monitoring and Management
- Early Mobility
Assessing and Managing Sedation

ABCDE

Awakening
Breathing
Coordination/Choice of Sedation
Delirium Monitoring and Management
Early Mobilization

ICU Sedation: The Balancing Act

Patient Comfort
and Ventilatory Optimization

Undersedation
- Patient recall
- Device removal
- Prolonged mechanical ventilation
- Initiation of neuromuscular blockade
- Myocardial or cerebral ischemia
- Decreased family satisfaction w/ care

Oversedation
- Prolonged mechanical ventilation
- Increased length of stay
- Increased risk of complications
- Increased diagnostic testing
- Unable to evaluate for delirium

Goal

Improper Sedation

- Continuous sedation carries the risks associated with oversedation and may increase the duration of mechanical ventilation (MV)
- MV patients accrue significantly more cost during their ICU stay than non-MV patients
  - $31,674 versus $12,931, P < 0.001
- Sedation should be titrated to achieve a cooperative patient and daily wake-up, a JC requirement

Assessing and Managing Sedation

Assessing Agitation and Sedation

- Sedation-Agitation Scale (SAS)
- Richmond Agitation-Sedation Scale (RASS)

Daily Sedation Interruption Decreases Duration of Mechanical Ventilation

- Hold sedation infusion until patient awake and then restart at 50% of the prior dose
- “Awake” defined as any 3 of the following:
  - Open eyes in response to voice
  - Use eyes to follow investigator on request
  - Squeeze hand on request
  - Stick out tongue on request
- Fewer diagnostic tests to assess changes in mental status
- No increase in rate of agitation-related complications or episodes of patient-initiated device removal
- No increase in PTSD or cardiac ischemia

ABC Trial: Objectives

- To determine the efficacy and safety of a protocol linking:
  - spontaneous awakening trials (SATs) & spontaneous breathing trials (SBTs)
    - Ventilator-free days
    - Duration of mechanical ventilation
    - ICU and hospital length of stay
    - Duration of coma and delirium
    - Long-term neuropsychological outcomes
Assessing and Managing Sedation

### ABC Trial: Main Outcomes

<table>
<thead>
<tr>
<th>Outcome</th>
<th>SBT</th>
<th>SAT+SBT</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ventilator-free days</td>
<td>12</td>
<td>15</td>
<td>0.02</td>
</tr>
<tr>
<td>Time-to-Event, days</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Successful extubation, days</td>
<td>7.0</td>
<td>5</td>
<td>0.05</td>
</tr>
<tr>
<td>ICU discharge, days</td>
<td>13</td>
<td>9</td>
<td>0.02</td>
</tr>
<tr>
<td>Hospital discharge, days</td>
<td>19</td>
<td>15</td>
<td>0.04</td>
</tr>
<tr>
<td>Death at 1 year, n (%)</td>
<td>97  (58%)</td>
<td>74 (44%)</td>
<td>0.01</td>
</tr>
<tr>
<td>Days of brain dysfunction</td>
<td>3.0</td>
<td>2.0</td>
<td>0.02</td>
</tr>
<tr>
<td>Coma</td>
<td>2.0</td>
<td>2.0</td>
<td>0.50</td>
</tr>
<tr>
<td>Delirium</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Median, except as noted


### ABC Trial: 1 Year Mortality

![Graph showing 1 Year Mortality](image)


### Despite Proven Benefits of Spontaneous Awakening/Daily Interruption Trials, They Are Not Standard of Practice at Most Institutions

- **Canada** – 40% get SATs (273 physicians in 2005)
- **US** – 40% get SATs (2004-05)
- **Germany** – 34% get SATs (214 ICUs in 2006)
- **France** – 40–50% deeply sedated with 90% on continuous infusion of sedative/opiate

---

Assessing and Managing Sedation

### ABCDE

- Awakening
- Breathing
- Coordination/Choice of Sedation
- Delirium Monitoring and Management
- Early Mobilization

---

### Characteristics of an Ideal Sedative

- Rapid onset of action allows rapid recovery after discontinuation
- Effective at providing adequate sedation with predictable dose response
- Easy to administer
- Lack of drug accumulation
- Few adverse effects
- Minimal adverse interactions with other drugs
- Cost-effective
- Promotes natural sleep

---

### Consider Patient Comorbidities When Choosing a Sedation Regimen

- Chronic pain
- Organ dysfunction
- CV instability
- Substance withdrawal
- Respiratory insufficiency
- Obesity
- Obstructive sleep apnea
Assessing and Managing Sedation

### GABA Agonist Midazolam

<table>
<thead>
<tr>
<th>Clinical Effects</th>
<th>Adverse Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>- Sedation, anxiolysis, and amnesia</td>
<td>- May accumulate with hepatic and/or renal failure</td>
</tr>
<tr>
<td>- Rapid onset of action (IV)</td>
<td>- Anterograde amnesia</td>
</tr>
<tr>
<td></td>
<td>- Long recovery time</td>
</tr>
<tr>
<td></td>
<td>- Synergy with opioids</td>
</tr>
<tr>
<td></td>
<td>- Respiratory depression</td>
</tr>
<tr>
<td></td>
<td>- Delirium</td>
</tr>
</tbody>
</table>

### GABA Agonist Propofol

<table>
<thead>
<tr>
<th>Clinical Effects</th>
<th>Adverse Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>- Sedation</td>
<td>- Pain on injection</td>
</tr>
<tr>
<td>- Hypnosis</td>
<td>- Respiratory depression</td>
</tr>
<tr>
<td>- Analgesia</td>
<td>- Hypotension</td>
</tr>
<tr>
<td>- Muscle relaxation</td>
<td>- Decreased myocardial contractility</td>
</tr>
<tr>
<td>- Mild bronchodilation</td>
<td>- Increased serum triglycerides</td>
</tr>
<tr>
<td>- Decreased ICP</td>
<td>- Tolerance</td>
</tr>
<tr>
<td>- Decreased cerebral metabolic rate</td>
<td>- Propofol infusion syndrome</td>
</tr>
<tr>
<td>- Anisometria</td>
<td>- Prolonged effect with high adiposity</td>
</tr>
<tr>
<td></td>
<td>- Seizures (rare)</td>
</tr>
</tbody>
</table>

### α2 Agonist Dexmedetomidine

<table>
<thead>
<tr>
<th>Clinical Effects</th>
<th>Adverse Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>- Antihypertensive</td>
<td>- Hypotension</td>
</tr>
<tr>
<td>- Sedation</td>
<td>- Hypertension</td>
</tr>
<tr>
<td>- Analgesia</td>
<td>- Nausea</td>
</tr>
<tr>
<td>- Decreased shivering</td>
<td>- Bradycardia</td>
</tr>
<tr>
<td>- Anxiolysis</td>
<td>- Dry mouth</td>
</tr>
<tr>
<td>- Patient arousability</td>
<td>- Peripheral vasoconstriction at high doses</td>
</tr>
<tr>
<td>- Potentiate effects of opioids, sedatives, and anesthetics</td>
<td>- Decrease sympathetic activity</td>
</tr>
</tbody>
</table>
Assessing and Managing Sedation

### Comparison of Clinical Effects

<table>
<thead>
<tr>
<th></th>
<th>Benzodiazepines</th>
<th>Propofol</th>
<th>Opioids</th>
<th>α₂ Agonists</th>
<th>Haloperidol</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sedation</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Alleviate anxiety</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Analgesic properties</td>
<td>X</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Promote arousability</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Facilitate ventilation</td>
<td>X</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Control delirium</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>


### Comparison of Adverse Effects

<table>
<thead>
<tr>
<th></th>
<th>Benzodiazepines</th>
<th>Propofol</th>
<th>Opioids</th>
<th>α₂ Agonists</th>
<th>Haloperidol</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prolonged weaning</td>
<td>X</td>
<td>X</td>
<td>X*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Respiratory depression</td>
<td>X</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypotension</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>Constipation</td>
<td></td>
<td>X</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Deltirionic</td>
<td>X</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tachycardia</td>
<td></td>
<td>morphine</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bradycardia</td>
<td></td>
<td>terfenadine</td>
<td>X</td>
<td>X</td>
<td></td>
</tr>
</tbody>
</table>

*Excluding remifentanil


### SEDCOM: Dexmedetomidine vs Midazolam

- Double-blind, randomized, multicenter trial comparing long-term (> 24 hr) dexmedetomidine (dex, n = 244) with midazolam (mz, n = 122)
- Sedatives (dex 0.2-1.4 µg/kg/hr or mz 0.02-0.1 mg/kg/hr) titrated for light sedation (RASS: -2 to +1), administered up to 30 days
- All patients underwent daily arousal assessments and drug titration O 4 hours

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Midazolam (n = 122)</th>
<th>Dexmedetomidine (n = 244)</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Time in target sedation range, % (primary EP)</td>
<td>75.1</td>
<td>77.3</td>
<td>0.18</td>
</tr>
<tr>
<td>Duration of sedation, days</td>
<td>4.1</td>
<td>3.5</td>
<td>0.01</td>
</tr>
<tr>
<td>Time to extubation, days</td>
<td>5.6</td>
<td>3.7</td>
<td>0.01</td>
</tr>
<tr>
<td>Delirium prevalence</td>
<td>93 (76.6%)</td>
<td>132 (54%)</td>
<td>0.001</td>
</tr>
<tr>
<td>Delirium-free days</td>
<td>1.7</td>
<td>2.5</td>
<td>0.002</td>
</tr>
<tr>
<td>Patients receiving open-labil midazolam</td>
<td>60 (49%)</td>
<td>150 (63%)</td>
<td>0.02</td>
</tr>
</tbody>
</table>

Reduced Delirium Prevalence with Dexmedetomidine vs Midazolam

SEDCOM Trial:
Safety Outcomes

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Midazolam (n = 122)</th>
<th>Dexmedetomidine (n = 244)</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bradycardia</td>
<td>18.9%</td>
<td>42.2%</td>
<td>0.001</td>
</tr>
<tr>
<td>Bradycardia needing treatment</td>
<td>0.9%</td>
<td>3.2%</td>
<td>0.07</td>
</tr>
<tr>
<td>Tachycardia</td>
<td>44.3%</td>
<td>25.4%</td>
<td>0.001</td>
</tr>
<tr>
<td>Hypertension requiring intervention</td>
<td>29.5%</td>
<td>18.9%</td>
<td>0.02</td>
</tr>
<tr>
<td>Hyperglycemia</td>
<td>42.6%</td>
<td>56.6%</td>
<td>0.02</td>
</tr>
<tr>
<td>Infections</td>
<td>19.7%</td>
<td>10.2%</td>
<td>0.02</td>
</tr>
</tbody>
</table>

Analgesedation

- Analgesic first (A-1), supplement with sedative
- Acknowledges that discomfort may cause agitation
- Remifentanil-based regimen
  - Reduces propofol use
  - Reduces median MV time
  - Improves sedation-agitation scores
- Not appropriate for drug or alcohol withdrawal
Assessing and Managing Sedation

Analgosedation

- 140 critically ill adult patients undergoing mechanical ventilation in single center
- Randomized, open-label trial
  - Both groups received bolus morphine (2.5 or 5 mg)
  - Group 1: No sedation (n = 70 patients) - morphine prn
  - Group 2: Sedation (20 mg/mL propofol for 48 h, 1 mg/mL midazolam thereafter) with daily interruption until awake (n = 70, control group)
- Endpoints
  - Primary
    - Number of days without mechanical ventilation in a 28-day period
  - Other
    - Length of stay in ICU (admission to 28 days)
    - Length of stay in hospital (admission to 90 days)


Analgosedation Results

- Patients receiving no sedation had
  - More days without ventilation (13.8 vs 9.6 days, \( P = 0.02 \))
  - Shorter stay in ICU (HR 1.86, \( P = 0.03 \))
  - Shorter stay in hospital (HR 3.57, \( P = 0.004 \))
  - More agitated delirium (N = 11, 20% vs N = 4, 7%, \( P = 0.04 \))
- No differences found in
  - Accidental extubations
  - Need for CT or MRI
  - Ventilator-associated pneumonia


ABCDE

Awakening
Breathing
Coordination/Choice of Sedation
Delirium Monitoring and Management
Early Mobilization
Assessing and Managing Sedation

Cardinal Symptoms of Delirium and Coma


ICU Delirium

- Develops in ~2/3 of critically ill patients
- Hypoactive or mixed forms most common
- Increased risk
  - Benzodiazepines
  - Extended ventilation
  - Immobility
- Associated with weakness
- Undiagnosed in up to 72% of cases

Patient Factors
- Increased age
- Alcohol use
- Male gender
- Living alone
- Smoking
- Renal disease

Environment
- Admission via ED or through transfer
- Isolation
- No clock
- No daylight
- Noise
- Physical restraints

Predisposing Disease
- Cardiac disease
- Cognitive impairment (e.g., dementia)
- Pulmonary disease

Acute Illness
- Length of stay
- Fever
- Medication service
- Lack of nutrition
- Hypotension
- Sepsis
- Metabolic disorders
- Medications
  - Anticholinergics
  - Corticosteroids
  - Benzodiazepines

Assessing and Managing Sedation

Mechanisms for Delirium in the Critically Ill Are Numerous and Not Clearly Understood

- Neurotransmitter imbalance
- Neuroinflammation
- Blood brain barrier permeability
- Impaired oxidative metabolism
- Microglial activation
- Abnormal levels of large neutral amino acids (e.g., tryptophan) and their metabolism (e.g., kynurenine pathway)

Sequelae of Delirium

- Increased mortality
- Longer intubation time
- Average 10 additional days in hospital
- Higher costs of care

- Increased mortality
- Development of dementia
- Long-term cognitive impairment
- Requirement for care in chronic care facility
- Decreased functional status at 6 months

Delirium Duration and Mortality

Kaplan-Meier Survival Curve

Each day of delirium in the ICU increases the hazard of mortality by 10%
Assessing and Managing Sedation

Worse Long-term Cognitive Performance

- Duration of delirium was an independent predictor of cognitive impairment
  - An increase from 1 day of delirium to 5 days was associated with nearly a 5-point decline in cognitive battery scores
- Patient testimony
  “One quite literally loses one’s grip on what is true and what is false because the true and the false are mixed together in a mess of experience.”


Risk Factors Specific for ICU Delirium

- Dementia
- Hypertension history
- Alcoholism
- Severity of illness
- Age
- Benzodiazepine use
- Coma (medical vs. pharmacologic)
- Morphine use
- Dementia
- Hypertension history
- Alcoholism
- Severity of illness
- Age


Delirium After Stroke

- Increased 12-month mortality risk
- Stroke patients +/- delirium
- Will delirium treatment change outcome?
Assessing and Managing Sedation

Intensive Care Delirium Screening Checklist

1. Altered level of consciousness
2. Inattention
3. Disorientation
4. Hallucinations
5. Psychomotor agitation or retardation
6. Inappropriate speech
7. Sleep/wake cycle disturbances
8. Symptom fluctuation

Score 1 point for each component present during shift
- Score of 1-3 = Subsyndromal Delirium
- Score of ≥4 = Delirium


Helpful Approach to Delirium Management

1. Stop
2. THINK
3. Lastly medicate

Stop and THINK

Do any meds need to be stopped or lowered?
- Especially consider sedatives
  - Is patient on minimal amount necessary?
    - Daily sedation cessation
    - Targeted sedation plan
  - Do sedatives need to be changed?

Toxic Situations
- CHF, shock, dehydration
- Delirigenic meds (tight titration)
- New organ failure (liver/kidney)

Hyoxemia
Infection/sepsis (nosocomial)
Immobilization
Nonpharm interventions
- Hearing aids, glasses, reorientation, sleep protocols, music, noise control, ambulation
K+ or electrolyte problems
**Delirium**

**Nonpharmacologic Interventions**

- **Early mobility** – the only nonpharmacologic intervention shown to reduce ICU delirium
- **Other interventions:**
  - Environmental changes (eg, noise reduction)
  - Sensory aids (eg, hearing aids, glasses)
  - Reorientation and stimulation
  - Sleep preservation and enhancement


**Sleep Abnormalities in the ICU**

- More time in light sleep
- Less time in deep sleep
- More sleep fragmentation


There is little evidence that sedatives in the ICU restore normal sleep.

**Boosting Sleep Quality in ICU**

- Optimize environmental strategies
  - Day/night variation, reduce night interruptions, noise reduction
- Avoid benzodiazepines (↓ SWS & REM)
- Consider dexmedetomidine (↑ SWS)
- GABA receptor agonists (eg, zolpidem)
- Sedating antidepressants (eg, trazodone) or antipsychotics
- Melatonin
  - Pilot: may improve sleep quality of ICU COPD patients

Assessing and Managing Sedation

Effect of Common Sedatives and Analgesics on Sleep
There is little evidence that administration of sedatives in the ICU achieves the restorative function of normal sleep

- Benzodiazepines
  - Stage 2 NREM
  - Slow wave sleep (SWS) and REM
- Propofol
  - Total sleep time without enhancing REM
  - SWS
- Analgesics
  - Abnormal sleep architecture
- Dexmedetomidine
  - SWS


Dopamine Antagonist Haloperidol

Clinical Effects
- Hypnotic agent with antipsychotic properties
  - For treatment of delirium in critically ill adults
- Does not cause respiratory depression

Adverse Effects
- Dysphoria
- Adverse CV effects include QT interval prolongation
- Extrapyramidal symptoms, neuroleptic malignant syndrome (rare)
- Metabolism altered by drug-drug interactions


But...Use of Haloperidol Is an Independent Predictor for Prolonged Delirium

**Assessing and Managing Sedation**

### Atypical Antipsychotics
- Receptor adherence is variable between agents
- Use has increased substantially
- Possible safety benefits
  - Decreased extrapyramidal effects
  - Little effect on the QTc interval (except ziprasidone)
  - Less hypotension/fewer orthostatic effects
  - Less likely to cause neuroleptic malignant syndrome
- Possible limitations
  - No IV formulations available
  - Little published experience in ICU patients
  - Troublesome reports of adverse events but most associated with prolonged use in non-delirium patients


### Prophylactic Haloperidol
- RCT of short-term low-dose IV haloperidol
- Patients
  - N = 457
  - Age > 65 years
  - ICU after noncardiac surgery
- Intervention
  - Haloperidol
    - 0.5 mg IV bolus then
    - Infusion 0.1 mg/h for 12 hrs
  - Placebo
- Primary endpoint
  - Incidence of delirium within the first 7 days after surgery


<table>
<thead>
<tr>
<th></th>
<th>Haloperidol (n = 229)</th>
<th>Placebo (n = 229)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>7 day delirium incidence (%)</td>
<td>15.3</td>
<td>23.2</td>
<td>0.031</td>
</tr>
<tr>
<td>Mean time to delirium onset (days)</td>
<td>6.2</td>
<td>5.7</td>
<td>0.021</td>
</tr>
<tr>
<td>Mean time delirium-free (days)</td>
<td>6.8</td>
<td>6.7</td>
<td>0.027</td>
</tr>
<tr>
<td>Median ICU LOS (hours)</td>
<td>21.3</td>
<td>23.0</td>
<td>0.024</td>
</tr>
<tr>
<td>All-cause 28-day mortality (%)</td>
<td>0.9</td>
<td>2.6</td>
<td>0.175</td>
</tr>
</tbody>
</table>

**Quetiapine vs. Placebo**

- Randomized, double-blind, placebo-controlled
- Multisite (3 centers)
- 36 ICU patients
- PO delivery of study drug
- Quetiapine dose: 50-200 mg q12h
- Primary outcome: time to first resolution of delirium (ie, first 12-hour period when ICDSC $\leq 3$)

**Quetiapine (n = 18)**
- Placebo (n = 18)

- Delirium + Haloperidol PRN

**Patients with First Resolution of Delirium**

Day During Study Drug Administration

Quetiapine added to as-needed haloperidol results in faster delirium resolution, less agitation, and a greater rate of transfer to home or rehabilitation.

**Impact of Quetiapine on the Resolution of Individual Delirium Symptoms**

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Median ICDSC and individual delirium symptoms similar at study baseline</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Quetiapine</td>
</tr>
<tr>
<td>Median time to symptom resolution</td>
<td>3 hrs</td>
</tr>
<tr>
<td>Inattention</td>
<td>9 hrs</td>
</tr>
<tr>
<td>Disorientation</td>
<td>4 hrs</td>
</tr>
<tr>
<td>Symptom fluctuation</td>
<td>5 hrs</td>
</tr>
<tr>
<td>Agitation</td>
<td>47 (19-67)%</td>
</tr>
</tbody>
</table>
Assessing and Managing Sedation

Before Considering a Pharmacologic Treatment for Delirium...

- Does your patient have delirium?
  - Assessed with scale?
- Which type of delirium?
  - Hyperactive
  - Hypoactive
  - Mixed hyperactive-hypoactive
- Have the underlying causes of delirium been identified and reversed/treated?
- Have non-pharmacologic strategies been optimized?


Antipsychotic Therapy

Rule Out Dementia

- Antipsychotic drugs are not approved for the treatment of dementia-related psychosis
  - No drug is approved for dementia-related psychosis
- Elderly patients with dementia-related psychosis treated with antipsychotic drugs are at an increased risk of death
- Physicians considering antipsychotics for elderly patients with dementia-related psychosis should discuss this increased risk of mortality with their patients, patients' families, and caregivers


ABCDE

- Awakening
- Breathing
- Coordination/Choice of Sedation
- Delirium Monitoring and Management
- Early Mobilization
Assessing and Managing Sedation

---

**Early Mobilization Protocol: Result**

- Return to independent functional status at discharge
  - 59% in intervention group
  - 35% in control group ($P = 0.02$)

---

**Early PT and OT in Mechanically Ventilated ICU Patients**

- All Patients

---

**Early Mobilization Patient Selection**

- **Inclusion criteria**
  - Medical ICU
  - Adults ($\geq 18$ years of age)
  - On MV $< 72$ h, expected to continue for at least $24$ h
  - Met criteria for baseline functional independence (Barthel Index score $\geq 70$)

- **Exclusion criteria**
  - Rapidly developing
    - Neuromuscular disease
  - Cardiopulmonary arrest
  - Irreversible disorders with estimated 6-month mortality $> 50$
  - Raised intracranial pressure
  - Absent limbs
  - Enrolment in another trial

---

Protocol for Early Mobility Therapy
Acute Respiratory Failure Patients

Early Mobility Therapy Results

Primary Endpoint: more protocol patients received PT than did usual care (80% vs. 47%, $P \leq 0.001$)

<table>
<thead>
<tr>
<th></th>
<th>Usual Care$^*$ (n = 135)</th>
<th>Protocol$^*$ (n = 145)</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Days to first out of bed</td>
<td>11.3</td>
<td>5.0</td>
<td>0.001</td>
</tr>
<tr>
<td>Ventilator days</td>
<td>10.2</td>
<td>8.8</td>
<td>0.163</td>
</tr>
<tr>
<td>ICU LOS days</td>
<td>6.9</td>
<td>5.5</td>
<td>0.025</td>
</tr>
<tr>
<td>Hospital LOS days</td>
<td>14.5</td>
<td>11.2</td>
<td>0.006</td>
</tr>
</tbody>
</table>

$^*$Values adjusted for BMI, Acute Physiology and Chronic Health Evaluation II, and vasopressors

Benefits of ABCDE Protocol

- Awakening & Uplifting Trial
- Coordination
- Liberation from ventilator
- Return ICU & Hospital discharge
- Activities to maintain brain function
- Early mobility, incentive
- Early mobility, vocational

- Early mobility, motor
- Early mobility, cognitive
- Early mobility, social
- Early mobility, psychological
- Early mobility, existential
Conclusions

• Oversedation in the ICU is common; associated with negative sequelae
• Analgosedation has been shown to improve outcomes; consider sedation only if necessary
• Use the ABCDE protocol
• Titrate all sedative medications using a validated assessment tool to keep patients comfortable and arousable if possible
• Use of benzodiazepines should be minimized

Conclusions

• Consider nonpharmacological management of delirium and reduce exposure to risk factors
• Typical and atypical antipsychotic medications may be used to treat delirium if nonpharmacological interventions are not adequate
• Early mobility in ICU patients decreases delirium and improves functional outcomes at discharge