Sedation in the ICU

Andrew Straznitskas, PharmD, BCCCP
Clinical Pharmacist, Medical ICU
NYC H+H/Bellevue
Contributors to ICU Agitation

- Anxiety
  - Sedatives

- Pain
  - Analgesics

- Delirium
  - Neuroleptics
Methods to Identify Delirium

- Intensive Care Delirium Screening Checklist (ICDSC)
  - Identify presence or absence of delirium
  - Score ≥ 4: + delirium
- Identify patients who may benefit from antipsychotics
- Minimize unnecessary treatment
# Intensive Care Delirium Screening Checklist (ICDSC)

<table>
<thead>
<tr>
<th>Step 1. Altered Level of Consciousness</th>
<th>Step 2. Inattention (1 point, if any of the following abnormalities present)</th>
</tr>
</thead>
<tbody>
<tr>
<td>A. Exaggerated response to normal stimulation (RASS +1 or greater) (1 point)</td>
<td>A. Difficulty in following commands OR</td>
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<tr>
<td>B. Normal wakefulness (RASS 0) (0 points)</td>
<td>B. Easily distracted by external stimuli OR</td>
</tr>
<tr>
<td>C. Response to mild or moderate stimulation (RASS -1 to -2) (1 point)</td>
<td>C. Difficulty in shifting focus</td>
</tr>
<tr>
<td>D. Patient recently received sedative/analgescia and (RASS -1 to -2) (0 points)</td>
<td>Does the patient follow you with their eyes?</td>
</tr>
<tr>
<td>E. Response only to intense and repeated stimulation (e.g. loud voice and pain) (RASS -3 to -4)</td>
<td></td>
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<tr>
<td><em>Stop Assessment</em></td>
<td><strong>Step 5. Psychomotor Agitation OR Retardation</strong> (1 point for each)</td>
</tr>
<tr>
<td>F. No response (RASS -5) <em>Stop Assessment</em> Based on primary caregiver assessment</td>
<td>A. Hyperactivity requiring the use of additional sedative drugs OR restraints in order to control potential danger (e.g. pulling IV lines out or hitting staff) OR</td>
</tr>
<tr>
<td><strong>Step 3. Disorientation</strong> (1 point for any one obvious abnormality)</td>
<td>B. Hypoactive or clinically noticeable psychomotor slowing or retardation Based on documentation and observation over shift by primary caregiver</td>
</tr>
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<td>A. Mistake in either time, place or person Does the patient recognize ICU caregivers who have cared for him/her and not recognize those who have not? What kind of place are you in?</td>
<td><strong>Step 6. Inappropriate Speech OR Mood</strong> (1 point for each)</td>
</tr>
<tr>
<td><strong>Step 4. Hallucinations OR Delusions</strong> (1 point for either)</td>
<td>A. Inappropriate, disorganized or incoherent speech OR</td>
</tr>
<tr>
<td>A. Equivocal evidence of hallucinations or a behavior due to hallucinations; hallucination: perception of something that is not there with NO stimulus OR</td>
<td>B. Inappropriate mood related to events or situation Is the patient apathetic to current clinical situation (i.e. lack of emotion)? Any gross abnormalities in speech or mood? Is the patient inappropriately demanding?</td>
</tr>
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<td>B. Delusions or gross impairment of reality testing; delusion: false belief that is fixed/unchanged</td>
<td><strong>Step 7. Sleep/Wake Cycle Disturbances</strong> (1 point for any one)</td>
</tr>
<tr>
<td>Any hallucinations now or over the past 24 hours? Are you afraid of the people or things around you? (Fear that is inappropriate to the clinical situation)</td>
<td>A. Sleeping less than four hours at night OR</td>
</tr>
<tr>
<td><strong>Step 8. Symptom Fluctuation</strong> (1 point, if present)</td>
<td>B. Waking frequently at night (do not include wakefulness initiated by medical staff or loud environment) OR</td>
</tr>
<tr>
<td>A. Fluctuation of any of the above items (i.e. steps 1-7) over 24 hours (e.g. from one shift to another) Based on primary caregiver assessment</td>
<td>C. Sleep greater than or equal to 4 hours during the day Based on primary caregiver assessment</td>
</tr>
<tr>
<td>Medication</td>
<td>Mechanism of Action</td>
</tr>
<tr>
<td>-------------</td>
<td>---------------------</td>
</tr>
<tr>
<td>Propofol</td>
<td>GABA+ NMDA-</td>
</tr>
<tr>
<td>Dexmedetomidine</td>
<td>Central α2 Agonist</td>
</tr>
<tr>
<td>Midazolam</td>
<td>GABA+</td>
</tr>
<tr>
<td>Lorazepam</td>
<td>GABA+</td>
</tr>
<tr>
<td>Ketamine</td>
<td>NMDA-</td>
</tr>
<tr>
<td>Fentanyl</td>
<td>Opioid</td>
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</table>
Propofol

• Pharmacologic Class: Sedative Hypnotic

• Mechanism of Action:
  • Stimulates GABA mediated sedation
  • NMDA receptor antagonism

• Dosing:
  • **Bolus**: 0.25-1 mg/kg
    • Relative Max: 100 mg
  • **Infusion**: 5-50 mcg/kg/min
    • Max: 75 mcg/kg/min
Propofol

• Pharmacokinetics
  • Onset: < 1 minute
  • Duration: < 10 minutes
    • May be slightly increased with prolonged infusions
  • Metabolism: Hepatic
  • Risk for Accumulation: Minimal

• Adverse Effects
  • Hypotension
  • Bradycardia
  • Respiratory Suppression
  • Hypertriglyceridemia
  • Propofol Infusion Syndrome (PRIS)
  • Green Urine (Benign)
  • Caloric Contribution (1.1 kcal/mL)
  • Soy/Egg Allergy
Dexmedetomidine

• Pharmacologic Class: Central $\alpha$-adrenergic agonist

• Mechanism of Action:
  • $\alpha$-adrenergic agonist in the locus ceruleus of the brain stem
  • Decreased central sympathetic output
  • Increased activity of inhibitory neurons.
  • $\alpha$-adrenergic agonist in the dorsal horn of the spinal cord (analgesia)

• Dosing
  • Loading Dose:
    • Not recommended; can cause significant bradycardia
    • 1 mcg/kg over 10 min
  • Infusion: 0.2-1 mcg/kg/hour
    • Relative Max: 1.5 mcg/kg/hour
Dexmedetomidine

• Pharmacokinetics
  • Onset (without Loading Dose): 20-30 minutes
  • Duration: 30-60 minutes
  • Metabolism: Hepatic
  • Risk for Accumulation: Minimal

• Adverse Effects
  • Bradycardia
  • Hypotension
  • No Respiratory Suppression
  • Withdrawal following Prolonged Use
    • Role for Clonidine
  • Rare:
    • Fever
    • HPA Suppression
    • Electrolyte Abnormalities
Midazolam & Lorazepam

• Pharmacologic Class: Benzodiazepine

• Mechanism of Action:
  • Stimulates GABA mediated sedation

• Dosing:
  • **Bolus**: 2-4 mg
  • **Infusion**: 1-10 mg/hr
    • Consider Bolus with Initiation and Dose Increases
  • Lorazepam 1 mg ≈ Midazolam 2 mg
    • Dose conversion of minimal clinical significance with prolonged infusion
Midazolam & Lorazepam

• Pharmacokinetics
  • Onset (Bolus):
    • Midazolam: 2-5 minutes
    • Lorazepam: 5-10 minutes
  • Duration (single dose):
    • Midazolam: 1-2 hours
    • Lorazepam: 2-4 hours
    • *Can be significantly longer (days-weeks) with prolonged infusion*
  • Metabolism:
    • Midazolam: Hepatic w/ Active Renal Metabolite
    • Lorazepam: Glucuronidation
  • Risk for Accumulation: Very High

• Adverse Effects
  • Hemodynamically Neutral
  • Respiratory Suppression
  • Delirium
  • Prolonged Sedation
  • Withdrawal following Prolonged Use
  • Propylene Glycol Toxicity (Lorazepam)
Ketamine

• Pharmacologic Class: NMDA Antagonist

• Mechanism of Action:
  • NMDA receptor antagonism
  • Disrupts connection within cortico-limbic system
  • “Dissociative” sedation
  • Modulates pain pathways, decreasing hyperalgesia, allodynia, and opioid tolerance

• Dosing
  • *Subanesthetic (Analgesic)*
    • **Bolus:** 0.1-0.3 mg/kg
    • **Infusion:** 0.1-0.3 mg/kg/hr
  • *Dissociative Sedation*
    • **Bolus:** 0.5-1 mg/kg
    • **Infusion:** 0.5-1.5 mg/kg/hr
Ketamine

• Pharmacokinetics
  • **Onset** (*Bolus*): < 1 minute
  • **Duration**: 10-20 minutes
    • *Recovery from Sedation*: 1-2 hours
  • **Metabolism**: Hepatic
  • **Risk for Accumulation**: Minimal

• Adverse Effects
  • **Hypertension/Tachycardia**
    • Due to Catechol Release
    • Contraindicated with Significant Cardiac Disease
  • **No Direct Respiratory Suppression**
    • Bronchodilatory
    • Positional Respiratory Inhibition
    • Potential Laryngospasm
  • **Emergence Reaction/Acute Psychosis**
  • **Nystagmus**
  • **Secretions (Oral/Ocular)**
Fentanyl

• Pharmacologic Class: Opioid Analgesic
• Mechanism of Action:
  • Binds to opioid receptors throughout CNS, increasing pain threshold and altering pain signal reception
  • Action in the CNS respiratory center directly suppresses respiratory drive
• Dosing
  • **Bolus**: 50-100 mcg
  • **Infusion**: 25-200 mcg/hr
    • Consider Bolus with Initiation and Dose Increases
Fentanyl

• Pharmacokinetics
  • **Onset** (*Bolus*): < 1 minute
  • **Duration** (*single dose*): 1-2 hours
    • *Can be significantly longer (days) with prolonged infusion*
  • **Metabolism**: Hepatic
  • **Risk for Accumulation**: Moderate-High

• Adverse Effects
  • Hemodynamically Neutral
  • Respiratory Suppression
  • Withdrawal following Prolonged Use
  • Constipation/Ileus
    • Start Bowel Regimen (Miralax+Senna) with Infusion
    • Deescalate as Appropriate
Monitoring Sedation in ICU

- Richmond Agitation-Sedation Scale (RASS)
- Important to titrate sedatives to objective measure of sedation
  - Must include goal in sedative order
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<td>Overtly combative, violent, immediate danger to staff</td>
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<td>+3</td>
<td>Very agitated</td>
<td>Pulls or removes tubes or catheters; aggressive</td>
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<td>Frequent non-purposful movement, fights ventilator</td>
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<tr>
<td>+1</td>
<td>Restless</td>
<td>Anxious but movements not aggressive; vigorous</td>
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<td>0</td>
<td>Alert and calm</td>
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<td>Briefly awakens with eye contact to voice (&lt; 10 seconds)</td>
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Sedation Goals

• Significant benefit with lighter levels of sedation
  • Shortened duration of mechanical ventilation
  • Decreased ICU and hospital length of stay
  • Lower risk of delirium/long term cognitive impairment

• Exceptions: Patients with requirement for deeper levels of sedation
  • ARDS
  • Patients requiring paralytics
  • Refractory status epilepticus
  • ICP Elevation
# RASS Score

## Richmond Agitation-Sedation Scale

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Strategies to Achieve Sedation Goals

• Analgosedation
• Prioritize Bolus Doses for Acute Symptoms
  • Benzodiazepines
  • Opioids
• Daily Sedation Interruptions
Analgosedation

- Providing adequate pain control can minimize sedation requirement
  - Avoid adverse effects of sedation
  - Minimize duration of sedation recovery
- Importance of pain assessment and treatment
Prioritize Bolus Dosing for Acute Symptoms

• Important strategy when using benzodiazepines and opioids
• Bolus more effective for control of acute agitation
  • Starting infusion of midazolam at 2 mg/hr it will take 1 hour to give 2 mg
• Uptitration of infusion rate without giving bolus can lead to excessive infusion rates and prolonged sedation
Daily Sedation Interruptions

• Holding sedation until patient awakens
  • Pair with Spontaneous Breathing Trial

• Restart sedation at 50% previous dose
  • Allow patient to demonstrate they need ongoing sedation

• Allows for neurological/pain assessment

• Minimize sedation accumulation

• Has been shown to decrease duration of mechanical ventilation and LOS
Questions