ICU Delirium: The “New” Organ Failure

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No disclosures

What is Delirium?
Acute neuropsychiatric syndrome affecting 15-80% of ICU patients
• Fluctuating disturbance in consciousness
• Acute confusion
• Cognitive and perceptual dysfunction
• Develops over short length of time

Dementia: intellectual deterioration over prolonged length of time

How Does it Manifest?
• Hyperactive delirium
  - 1/3 of patients
• Hypoactive delirium
  - 2/3 of patients

What are the Signs?
- Patient may be awake and conversant, but …
- Global cognitive dysfunction (may be subtle, missed)
  - loss of short-term memory, understanding
- Disorientation, inattention
  - unable to make sense of environment
  - unable to problem-solve, self-care
- Confuses reality, dream-state
  - visual, tactile, auditory hallucinations
  - abnormal movements, picking (hyperactive delirium)

What Increases Delirium Risk?
- Advanced age, cognitive impairment
- Co-morbidity (multisystem disease)
- Acute illness (sepsis, ARDS, etc)
- Major surgery (CT, vascular, trauma, Tx etc)
- Medications with anticholinergic activity
  - opioids, benzodiazepines, H2 antagonists
- Drug withdrawal syndromes
  - alcohol, nicotine, psychotropic medications

Patient and Illness Factors

- Anxiety and pain
- Overmedication
  - anxiolytics, sedatives, analgesics, antipsychotics
- Prolonged immobility
  - restraints, delayed mobilization
  - disuse, wasting, critical illness myopathy
- Incipient noise, noxious sensations
  - vital signs, laboratory tests, X-rays
  - loss of day-night / sleep-wake rhythm
  - disorientation for time, place, circumstances

ICU Environmental Factors

Consequences of ICU Delirium

- Increased postoperative complications
- Increased ICU and hospital LOS
- Increased hospital mortality
- Increased one-year mortality
- Post intensive care syndrome (PICS)
One Year Mortality
- 919 hospitalized patients over 3-yr period
- 62% increase in risk of mortality
- 13% decrease in 1-yr survival

Post Intensive Care Syndrome (PICS)
Girard TD et al & Myhren H et al. Crit Care Med 2010;38;1513-20, 1554-61
- Prolonged effects after discharge
- Permanent cognitive dysfunction
- Impaired basic problem solving:
  - daily activities, multi-tasking, judgment
- Short term memory loss:
  - impaired attention, social conversation

Post Intensive Care Syndrome (PICS)
Girard TD et al & Myhren H et al. Crit Care Med 2010;38;1513-20, 1554-61
- Loss of independent daily self-care
- Unable to return to work (>50%)
- Depression (>45%)
- High risk of nursing home placement
- Increased burden on family, caregivers
- Financial cost to patient, family, survivors

How Do We Diagnose and Assess ICU Delirium?

Delirium Assessment
Confusion Assessment Method for the ICU (CAM-ICU)
Intensive Care Delirium Screening Checklist (ICDSC)

CAM-ICU
Assess level of sedation (RASS)
Assess for delirium (CAM-ICU)

Richmond Agitation-Sedation Scale (RASS)
Sessler CN et al. Am J Respir Crit Care Med 2002; 166:1338-44
Step 1: Observe patient
alert, calm 0
restless, agitated, violent, combative +1 to +4
Step 2: Command eye contact
sustained eye contact (> 10 sec) -1
non sustained eye contact (< 10 sec) -2
moves but no eye contact -3
Step 3: Physical stimulation
movement response only -4
no response -5

CAM-ICU Positive
1. Acute or fluctuating decline in mental status
and
2. Inattention
and either
3. Altered Level of Consciousness
or
4. Disorganized Thinking

Visual Attention
www.icudelirium.org

Delirium CRASH 2-16 V2 - March 2, 2016
### Disorganized Thinking

<table>
<thead>
<tr>
<th>Question</th>
<th>Answer</th>
</tr>
</thead>
<tbody>
<tr>
<td>Will a leaf float on water?</td>
<td>No</td>
</tr>
<tr>
<td>Are there fish in the sea?</td>
<td>Yes</td>
</tr>
<tr>
<td>Does one pound weigh more than two pounds?</td>
<td>No</td>
</tr>
<tr>
<td>Can you use a hammer to pound a nail?</td>
<td>Yes</td>
</tr>
</tbody>
</table>

#### ICDSC

<table>
<thead>
<tr>
<th>Component</th>
<th>No</th>
<th>Yes</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Consciousness altered: agitation, somnolence (SASS or RASS)</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>3. Disorientation: “what kind of place is this?”</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>4. Hallucination, delusion, psychosis</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>5. Psychomotor agitation or retardation</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>6. Inappropriate speech or mood</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>7. Sleep-wake cycle disturbance</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>8. Fluctuation of symptoms</td>
<td>0</td>
<td>1</td>
</tr>
</tbody>
</table>

- RN summarizes score for **entire shift**
  - adds total number of positive components
  - one is positive even if it resolves during shift
- Excessive sedation - unable to assess
- List positive components (C, A, D, H, P, I, S, F)
- Score ≥ 4 = delirium
- Score 1-3 = subsyndromal delirium (high risk)

### How Do We Treat or Prevent ICU Delirium?

#### Pharmacologic Therapy for ICU Delirium

**Pharmacologic**

- Assess and Treat Pain

#### Non-pharmacologic

- Pharmacologic Treatment of ICU Delirium

### Assess and Treat Pain

**Assess and Treat Pain**

#### Opioids

<table>
<thead>
<tr>
<th>Opioid</th>
<th>Lipid Solubility</th>
<th>Histamine Release</th>
<th>Potency</th>
</tr>
</thead>
<tbody>
<tr>
<td>Morphine</td>
<td>+/-</td>
<td>+++</td>
<td>1</td>
</tr>
<tr>
<td>Hydromorphone</td>
<td>+</td>
<td>++</td>
<td>5</td>
</tr>
<tr>
<td>Fentanyl</td>
<td>+++</td>
<td>0</td>
<td>50</td>
</tr>
</tbody>
</table>

### Opioid-Sparing Multimodal Therapy

- Thoracic epidural analgesia
  - fentanyl-bupivacaine infusions
- Dexmedetomidine 0.1-1.4 mcg/kg/hr
  - anxiolysis, analgesia without respiratory depression
  - attenuates catecholamine response (bradycardia)
- Lidocaine patch
- Ketamine infusion 1-5 mcg/kg/min
- Gabapentin: start at 100 mg VT or PO tid
Benzodiazepines

<table>
<thead>
<tr>
<th>Generic</th>
<th>Trade Names</th>
<th>Approved</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chlordiazepoxide</td>
<td>Librium®</td>
<td>1965</td>
</tr>
<tr>
<td>Oxazepam</td>
<td>Serax®</td>
<td>1965</td>
</tr>
<tr>
<td>Lorazepam</td>
<td>Ativan®</td>
<td>1977</td>
</tr>
<tr>
<td>Temazepam</td>
<td>Restoril®</td>
<td>1981</td>
</tr>
<tr>
<td>Alprazolam</td>
<td>Xanax®</td>
<td>1981</td>
</tr>
<tr>
<td>Midazolam</td>
<td>Versed®</td>
<td>1985</td>
</tr>
<tr>
<td>Zolpidem</td>
<td>Ambien®</td>
<td>1992</td>
</tr>
</tbody>
</table>

The Safety and Efficacy of Dexmedetomidine Compared to Midazolam (SEDCOM)

Riker RR et al. JAMA 2009; 301:489-99

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Dexmedetomidine (n = 244)</th>
<th>Midazolam (n = 122)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Time at target RASS</td>
<td>77.3%</td>
<td>75.1%</td>
</tr>
<tr>
<td>Median time to tracheal extubation</td>
<td>3.7 days</td>
<td>5.6 days*</td>
</tr>
<tr>
<td>ICU LOS</td>
<td>5.9 days</td>
<td>7.6 days</td>
</tr>
<tr>
<td>Delirium (CAM-ICU)</td>
<td>54%</td>
<td>76.6%</td>
</tr>
</tbody>
</table>

Lorazepam and Delirium


Incremental risk of delirium increases with dose of lorazepam over previous 24 hours
Dose > 20 mg = 100% incidence

Propofol

\[ \text{di-iso-propylphenol} \]

\[
\begin{array}{c}
\text{(CH}_3\text{)}_2\text{CH} \\
\text{CH(CH}_3\text{)}_2
\end{array}
\]

Propofol Dose-Response

<table>
<thead>
<tr>
<th>Infusion Rate µg/kg/min</th>
<th>Pharmacodynamic Effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt; 100</td>
<td>anesthetic</td>
</tr>
<tr>
<td>5-30</td>
<td>sedative-hypnotic</td>
</tr>
<tr>
<td>2-5</td>
<td>anxiolytic</td>
</tr>
<tr>
<td>1-2</td>
<td>anti-emetic</td>
</tr>
</tbody>
</table>

Propofol Infusion Syndrome (PRIS)


- First reported in children < 5 yrs
- Long-term propofol infusion > 50-75 µg/kg/min
- Refractory shock:
  - cardiac failure, rhabdomyolysis, acidosis, AKI
- Risk factors:
  - acute CNS / inflammatory disease / sepsis
  - catecholamines and/or steroids
- Pathogenesis:
  - impaired FFA utilisation / mitochondrial activity

Antipsychotics

<table>
<thead>
<tr>
<th>Generic</th>
<th>Trade Names</th>
<th>Approved</th>
</tr>
</thead>
<tbody>
<tr>
<td>Haloperidol</td>
<td>Haldol®</td>
<td>IM only</td>
</tr>
<tr>
<td>Droperidol</td>
<td>Inapsine®</td>
<td>Black box</td>
</tr>
<tr>
<td>Aripiprazole</td>
<td>Abilify®</td>
<td>1992</td>
</tr>
<tr>
<td>Quetiapine</td>
<td>Seroque®</td>
<td>1997</td>
</tr>
<tr>
<td>Olanzepine</td>
<td>Zyprexa®</td>
<td>2009</td>
</tr>
</tbody>
</table>

No antipsychotic is approved for delirium
Agitation & Delirium in Adult ICU

Dopaminergic withdrawal to alcohol or benzodiazepine patients, suggest using dexmedetomidine when sedation is required in delirious ventilated adult patients.

Suggest using either propofol or dexmedetomidine rather than

Neurochemical Balance

- Alpha-2 Adrenoceptors
- Receptor Binding Profiles
- Adverse Effects of Antipsychotics

Non-Pharmacologic Therapy to Prevent or Ameliorate Delirium

Clinical Practice Guidelines for Pain, Agitation & Delirium in Adult ICU

- Decrease noise, light, interventions
- Restore natural sleep, day-night rhythm
- Enhance ICU ADL, avoid restraints
- Family exposure and support
- Early mobilization, PT and OT
- Enhance communication, orientation - cognitive stimulation (iPad therapy)

Non-Pharmacologic Therapy

Multicomponent Therapy

- Suggest using either propofol or dexmedetomidine rather than benzodiazepines for mechanically ventilated adult patients
- When sedation is required in delirious patients, suggest using dexmedetomidine rather than benzodiazepines (unless due to alcohol or benzodiazepine withdrawal)

“Cooperative Sedation”

Richard Riker, MD Maine Medical Center

Supplemental digital content is available for this article. Direct URL citations appear in the printed text and are provided in the HTML and PDF versions of this article. The articles can be accessed using the URLs listed in the “Supplemental digital content” section of this article.
ICU Activities of Daily Living

- Communication with family, caregivers
- Oral suctioning, toilet
- Pressing a call bell, attracting attention
- Self-feeding, grooming
- Using smartphone, TV remote
- Incentive spirometry, exercise

Multicomponent Therapy


- 169 patients pre- and 171 post-intervention
- Multicomponent bundle of interventions
- Subjective ranking of noise, light, nurse interventions
- Delirium by CAM-ICU

ABCDE Bundle


- Awakening and Breathing Coordination
  - coordinated spontaneous awakening, breathing trials (SAT, SBT)
- Delirium, sedation/agitation monitoring and management
- Early progressive exercise and mobilization

“Tablet Therapy”

- Communication by touch-screen, stylus
  - propping device (wedge pillow)
- Interactive apps (relaxing/stimulating programs)
  - music, breathing, muscle relaxation, meditation
  - leisure activities, spiritual needs
  - social, news media
- Manual dexterity
  - fine motor coordination
- Educational handbook
  - patients, family members, caregivers