ICU Updates: Delirium in Hospitalized Patients

Recognizing and preventing delirium to improve patient outcomes

No conflicts of interest or financial disclosures
Possible off-label use of medications for delirium will be discussed

Outline

• Delirium defined
• What causes delirium?
• Prevalence of the problem
• Outcomes and costs
• Recognizing delirium
• Treatment and prevention

Case 1

• A 79-year-old woman develops confusion. She is in the ICU with community acquired pneumonia and required mechanical ventilation for 2 days & received lorazepam IV at that time. She was extubated yesterday.
• She was clearer immediately after extubation, but now she is disoriented and is saying things that do not make sense according to her family. At baseline, she lives alone and is independent. She does not drink alcohol.
• MEDS: Ertapenem, azithromycin, HCTZ, atenolol, senna, docusate, and PRN lorazepam and morphine
• PE: Vitals are normal. Neurologic exam is non-focal, and cranial nerve exam is normal. She is calm and awake but cannot follow commands. Denies that she is seeing things or hearing things that are not there, but appears easily distracted and seems to be talking to someone who is not present. Laboratory studies show HCT 30. WBC 10 (down from 15). Metabolic panel reveals plasma glucose of 160 mg/dL, TSH is normal, UA is bland

Case 1

Which of the following is the most likely diagnosis?

• A. Over-sedation
• B. Dementia
• C. Psychosis
• D. Stroke
• E. Delirium
Delirium

Which of the following is MOST consistent with a diagnosis of delirium?

1. Ability to shift attention quickly.
2. Fluctuation in cognition over hours.
3. That toxic, metabolic and structural lesions have been ruled out.
4. Hyperactivity without evidence of hypoactivity.
5. Lack of evidence of depression.

Delirium defined

- Reversible, acute brain dysfunction
  - May persist for weeks or more
- Acute waxing and waning mental status
  - Somnolence
  - Agitation (may be absent or minor feature only)
  - Normal
- Inattention, distractibility
- Disorganized thinking
  - Disorientation
  - Memory problems
  - Incoherent speech, non-purposeful behavior

Case 2

- A 83-year-old man was hospitalized 5 days ago after a left hip fracture with surgical repair 4 days ago. As his alertness has increased over the past days, he has become more agitated, yelling and flailing his arms. Soft restraints were placed 2 days ago. He has a 5-year history of Alzheimer dementia.
- MEDS: Acetaminophen, memantine, diphenhydramine, metoprolol, and low-molecular-weight heparin.
- PE: Afebrile, BP 110/65 mmHg, HR 100/min, respiration rate is 18/min, 95% on 2L O2. The patient can move all extremities. He is inattentive, oriented only to person, and exhibits combativeness alternating with hypersomnolence. The remainder of the neurologic examination is unremarkable (no focal findings).

Case 2

- Which of the following is the most likely diagnosis?
  - A. Embolic CVA
  - B. Acute exacerbation of dementia
  - C. Meningitis
  - D. Postoperative delirium
Delirium Prevalence

Which setting has the highest reported rates of delirium?
1. ICU 70%
2. ED 10%
3. Hospice 42%
4. PACU 16%

Prevalence of ICU Delirium

- 50-80% of ventilated patients
- Even 20-50% of lower severity score ICU patients
- 10% remain delirious at hospital discharge

Ely EW JAMA 2001;286:2703
Ely EW JAMA 2004;291:1753
Ely EW CCM 2001;29:1370
Ely EW CCM 2004;32:106
Micek S CCM 2005;33:1260
Thomason J Crit Care 2005;9:375
McNicoll L JAGS 2003;51:591

Delirium is often invisible in ICU

- Most ICU delirium is hypoactive subtype (35%) or mixed (64%)
- PURE hyperactive subtype is rare
- Older age is a strong predictor of hypoactive type
- Onset ICU Day 2 (+/- 1.7 days)

Prevalence of Delirium in ICU

- Hypoactive delirium
- Mixed delirium
- Hyperactive delirium

Peterson J. JAGS 2006;54: 479
Delirium: Causes

In the ICU, most cases of delirium can be attributed to a single cause.
1. True
2. False

ICU delirium = convergence of many risks

Common ICU themes =
- Polypharmacy
- Liver failure
- Infection
- Kidney failure
- Dehydration
- Hypoxemia/hypercapnia
- Pain
- Immobility
- CNS insults (e.g. stroke)
- Malnutrition (deficiencies)
- Bladder catheters
- ETOH withdrawal
- Sleep deprivation
- Circadian disarray

Risks for delirium

50% Prior CVA or Dementia

Delirium Risk Factors

Delirium = disturbance of global cortical function
Case 3

- 77-year-old woman is admitted to the ICU for CHF exacerbation. She developed worsening shortness of breath and hypoxemia over 3 weeks, associated with a 20 pound weight gain and increased lower extremity edema. After 3 days of medical therapy and CPAP for one day, her oxygenation has improved and her weight has decreased 12 pounds. While assessing her for transfer out of the ICU you find her slow to respond to questions, oriented only to person, and inconsistently following commands. Yesterday her mental status seemed normal and she asked you several questions about her planned stay in a rehab facility after hospital discharge. VS stable. Exam and labs show no changes from yesterday except Cr 1.2 down from 1.5. No other abnormalities. ECG is unchanged.

Which of the following is true regarding her prognosis?

A. Controlling for other factors, her mental status change has no independent bearing on her future prognosis
B. Her delirium will result in longer hospital stay but does not influence mortality
C. The presence of delirium is an independent predictor of mortality
D. No change in care is necessary, delirium will improve on its own

How does ICU delirium affect survival and LOS?

Ely EW et al. JAMA. 2004;291:1753-1762
Financial cost of delirium (by severity)

<table>
<thead>
<tr>
<th></th>
<th>ICU Cost</th>
<th>Hospital Cost</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild</td>
<td>$0</td>
<td>$23,000</td>
</tr>
<tr>
<td>Moderate</td>
<td>$10,000</td>
<td>$42,000</td>
</tr>
<tr>
<td>Severe</td>
<td>$20,000</td>
<td>$50,000</td>
</tr>
</tbody>
</table>

Milbrandt E et al. CCM 2004;32:955

Case 4

- A 68-year-old man with a history of cirrhosis and COPD is being weaned from mechanical ventilation after an exacerbation. His current medications are ipratropium bromide and albuterol, prednisone, and azithromycin.
- He had an unsuccessful spontaneous breathing trial yesterday morning with agitation, tachypnea and oxygen desaturation. He was given lorazepam 1mg IV for sedation and volume-controlled ventilation was resumed. He received two more doses of lorazepam over the past 24h. Today he is calm but is not able to follow commands consistently.

Which of the following is the best test to assess the patient’s mental status?

A. Serum ammonia level
B. Confusion Assessment Method for the Intensive Care Unit (CAM-ICU)
C. CT scan of the head
D. Metabolic cart testing for VCO2
E. Mini-Mental State Examination

Delirium Recognition:

1. New onset fluctuating mental status OR Acute mental status/behavioral change
   AND
   - Inattention

2. Disorganized thinking OR Altered Level of Consciousness

Ely EW JAMA 2001;286:2703
Confusion Assessment Method for the ICU (CAM-ICU)

1. Change/fluctuating mental status last 24h
   - Yes → No Delirium
   - No

2. Inattention: < 8/10 commands followed
   - Yes → No Delirium
   - No

3. Disorganized Thinking: Unable to do sequential command or cognitive problem
   - Yes → No Delirium
   - No

   OR
   Altered Level of Consciousness (right now) (RASS other than 0)
   - Yes → Delirium
   - No

Delirium Present, Now What?

Workup, Differential
- Hx, Vitals, Exam, Basic Labs, UA, ECG
- ANY Meds?
- Lytes/dehydration
- Toxidrome? (Utox, 7WD)
- Exam (focal neuro findings?)
- Respiratory (O2, CO2)
- Endocrine (Glucose, TSH)
- Deficiencies (B12/folate)

Environmental Interventions

Safety a Concern? Consider Meds

Richmond Agitation & Sedation Scale

<table>
<thead>
<tr>
<th>Scale</th>
<th>Label</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>+4</td>
<td>COMBATIV</td>
<td>Combative, violent, immediate danger to staff</td>
</tr>
<tr>
<td>+3</td>
<td>VERY AGITATED</td>
<td>Pulls to remove tubes or catheters; aggressive</td>
</tr>
<tr>
<td>+2</td>
<td>AGITATED</td>
<td>Frequent non-purposeful movement, fights ventilator</td>
</tr>
<tr>
<td>+1</td>
<td>RESTLESS</td>
<td>Anxious, apprehensive, movements not aggressive</td>
</tr>
<tr>
<td>0</td>
<td>ALERT &amp; CALM</td>
<td>Spontaneously pays attention to caregiver</td>
</tr>
<tr>
<td>-1</td>
<td>DROWSEY</td>
<td>Not fully alert, but has sustained awakening to voice (eye opening &amp; contact &gt;10 sec)</td>
</tr>
<tr>
<td>-2</td>
<td>LIGHT SEDATION</td>
<td>Briefly awakens to voice (eyes open &amp; contact &lt;10 sec)</td>
</tr>
<tr>
<td>-3</td>
<td>MODERATE SEDATION</td>
<td>Movement or eye opening to voice (no eye contact)</td>
</tr>
</tbody>
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If RASS is 2-3 proceed to CAM-ICU (is patient CAM-ICU positive or negative?)

-4 DEEP SEDATION No response to voice, but movement or eye opening to physical stimulation
-5 UNARouseable No response to voice or physical stimulation

Environmental Interventions

Delirium Treatment AND Prevention
- Sleep protocol (non-pharmacologic)
- Cognitively-stimulating activities
- Reorientation, repeated (family, sitter)
- Early mobilization & range of motion
- Adequate Hydration
- Minimize Noise (?ear plugs)
- Eye glasses and hearing aids
- Remove restraints & catheters
- Scheduled Pain Protocol
Preventing delirium? Factors you can’t control...

Factors you can...

Sedatives... A “cause” or “because” of delirium...

Case 5

- A 75-year-old man with a history of HTN, CAD, CHF, paroxysmal Afib is evaluated in the ICU for delirium. He had an open aortic valve replacement and was extubated on POD 2. Two days later he developed fluctuations in his mental status and inattention. He became agitated, pulling at lines, attempting to climb out of bed, and asking to leave the hospital. He has no history of alcohol abuse. His lab values are normal. The use of frequent orientation cues, calm reassurance, and the presence of family has not improved the patient’s agitation.
Case 5

Which of the following is the most appropriate therapy for this patient's delirium?
- A. Diphenhydramine
- B. Haloperidol
- C. Lorazepam
- D. Dexmedetomidine

When to use pharmacotherapy for delirium

- Activated symptoms that interfere with patient safety may require medical therapy
- Should be in concert with environmental interventions
- Should be in conjunction with thorough review of all meds

Choices: Haldol

- Published recommendations are empiric
- Common choice for ICU delirium (little data)
- Minimal respiratory depression
- Starting dose 1 mg IV (.5 mg in elderly) PO is OK
- Sedation typically in 1 hour, but long half-life (13-35 hours), multiple doses → over sedation

Haldol

- Dose dependent increase in QTc (>450ms = worry)
- Extrapyramidal side effects
- Neuroleptic malignant syndrome

Remember co-offenders:
MACROLIDES
AMIODARONE
 METHADONE MANY OTHERS!

Check baseline and follow
Alternatives: Quetiapine

36 delirious ICU patients
prn Haldol

50 mg Quetiapine (Seroquel) q 12

Placebo

Needed fewer days of Haldol but no decrease in extrapyramidal side effects, QT prolongation, or ICU LOS. Increase in somnolence.


Alternatives: Ziprasidone

101 mechanically vented ICU patients
q12 hours

Ziprasidone
Haldol
Placebo

No decrease in delirium, delirium free days, ventilator free days, or ICU LOS

Both are pilot studies. Cochrane analysis in 2009: no large studies & no clear superiority between haloperidol, risperidone, olanzapine. High-dose haloperidol has much more EPS.


Case 5 - continued

• The same 75-year-old patient has been continuously delirious. He continues to have a full-time sitter and is receiving quetiapine 50mg QAM and 100 mg QPM, haloperidol 1 mg q2h PRN, clonazepam 1 mg TID, midazolam 0.5 mg Q2h PRN. He is pulling out his lines and had a fall out of bed this morning while trying to get up.

Case 5

Which of the following is the best next therapy for this patient’s delirium?

• A. Clonidine
• B. Stop all meds
• C. Labatolol
• D. Quetiapine
• E. Dexmedetomidine
Central alpha-2 agonists

- **Dexmedetomidine**
  - Associated with less delirium when used for sedation vs benzodiazepines
  - Achieves same sedation goals as propofol and benzodiazepines up to RASS -3
  - Associated with shorter duration of ventilation
  - Less well studied in delirium treatment
  - Not associated with shorter ICU stay
  - Induces bradycardia
  - Decreases cerebral blood flow

- **Clonidine**
  - Less well studied, but may have benefits

Post talk test
Which of the following best describes the effects of critical illness on physiologic sleep?

A. Opiate-benzodiazepine combos promote physiologic sleep in patients on ventilators
B. The proportion of REM sleep is decreased
C. Sleep has predominant waveforms consistent with deep sleep
D. Total duration of sleep during a 24-hour period is increased

Take home points

**Delirium**
- A symptom of acute organ (brain) dysfunction
- Characterized by fluctuating mental status
- Common, but is often unrecognized
- Is an independent risk for poor outcomes
- Prevention first – especially in high risk patients
- Sedative & analgesic plan – minimize & avoid offenders (benzodiazepines)
- Antipsychotics can be useful in agitated delirium
- Identification of delirious patients before transfer out of the ICU can impact subsequent care