Dazed and Confused in the Intensive Care Unit: Managing Delirium Is More Than Just a State of Mind

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Disclosure

The program chair and presenters for this continuing education activity have reported no relevant financial relationships.
Objectives

- Describe potential mechanisms of benzodiazepine (BZD)-induced ICU delirium

- Review published clinical trials evaluating ICU delirium outcomes with BZD exposure

- Evaluate the strength of evidence associating ICU delirium with BZD use
Patient Case

- 65 y.o. male MSSA sepsis with developing PNA 5 days previously on mechanical ventilation w propofol / fentanyl
- PMHx: heroin IVDA (methadone), MSSA IE
- Transferred from OSH for possible ECMO 2/2 worsening ARDS
- Broad spectrum abx (cefepime, vancomycin and tobramycin)
- Propofol titrated to 75 mcg/kg/min and fentanyl @ 400mcg/hr => RASS -3 to -2
- Vent settings optimized -> dysynchrony without gas exchange improvement
- Cisatracurium considered
Patient Case

**FAST FORWARD 7 DAYS**

- Midazolam and cisatracurium ordered -> no improvement
- ECMO -> decannulated after ~5 days
- Sedation has been titrated down – propofol and fentanyl
- CAM-ICU assessment now positive (RASS -3)
How confident are you that midazolam is the sole and primary cause of ICU delirium?

- **A** YES – midazolam is the cause
- **B** NO – midazolam is NOT the source
- **C** MAYBE – midazolam could be playing a role, but not clear
Independent Risk Factors
## Lorazepam: Independent Risk Factor

### Multivariable Analysis for Transitioning to Delirium/Coma or Delirium Only

<table>
<thead>
<tr>
<th>Medication</th>
<th>Odds Ratio (95% CI)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lorazepam</td>
<td>1.2 (1.1 – 1.4)</td>
<td>0.003</td>
</tr>
<tr>
<td>Midazolam</td>
<td>1.7 (0.9 – 3.2)</td>
<td>0.09</td>
</tr>
<tr>
<td>Fentanyl</td>
<td>1.2 (1.0 – 1.5)</td>
<td>0.09</td>
</tr>
<tr>
<td>Morphine</td>
<td>1.1 (0.9 – 1.2)</td>
<td>0.24</td>
</tr>
<tr>
<td>Propofol</td>
<td>1.2 (0.9 – 1.7)</td>
<td>0.18</td>
</tr>
</tbody>
</table>

### Lorazepam & Delirium Transition Probability

- **Medication**: Lorazepam
- **Dose (mg)**: \( \leq 24 \) hours
- **Probability of Delirium**
- **Graph**: Transition probability over lorazepam dose (mg) within 24 hours.

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*Pandharipande P. Anesthesiology 2006;104:21-6*
Drug-induced Risk Factors

Non-users of analgesia/sedation

ICU Patient Population

Surgical  Trauma  Surgical  Trauma  Surgical  Trauma

Days Delirious (%)

Midazolam

Fentanyl

Morphine

p=0.014  p=0.031  p=0.007  p=0.936  p=0.069  p=0.024

Surgical  Trauma  Surgical  Trauma  Surgical  Trauma

Pandharipande P. J Trauma 2008;65:34-41
Pharmacologic-based Mechanism
Delirium Pathophysiology

- Dopamine
- Serotonin
- Cortisol
- Glutamate
- GABA
- Cholinergic
8-Hour Sleep Cycle

Weinhouse GL. Sleep 2006;29:707-16
Weinhouse GL. Anesthesiology Clin 2011;29:675-685
# Sedation & Analgesia Impact on Sleep

<table>
<thead>
<tr>
<th>Agents</th>
<th>Effects on Sleep</th>
</tr>
</thead>
</table>
| Opiates         | • ↓ REM  
                    • ↓ Stage 3 & 4                                                             |
| Benzodiazepines | • ↓ REM  
                    • ↓ Stage 3 & 4 (elimination with continued use)                           |
| Propofol        | • ↑ Sleep latency  
                    • ↓ Stage 3 & 4?  
                    • No interference with “restorative effects” of natural sleep            |
| Dexmedetomidine | • Similar to natural sleep  
                    • EEG activity suggest similar to Stage 2  
                    • Enhance deep sleep (Stage 3 & 4?)                                        |

Weinhouse GL. Sleep 2006;29:707-16
Weinhouse GL. Anesthesiology Clin 2011;29:675-685
8-Hour Sleep Cycle

REM = Rapid Eye Movement

Weinhouse GL. Sleep 2006;29:707-16
Weinhouse GL. Anesthesiology Clin 2011;29:675-685
Connecting the Dots…

- Sedation ≠ sleep
- Experimental models of sleep fragmentation and deprivation may lead similar clinical manifestations as total sleep deprivation (i.e. delirium)
- Sleep deprivation → ICU delirium?
- So can we assume the following…

Delirium Risk

- Benzodiazepines
- Propofol
- Dexmedetomidine

Weinhouse GL. Sleep 2006;29:707-16
Weinhouse GL. Anesthesiology Clin 2011;29:675-685
Do you consider benzodiazepines more deliriogenic than propofol or dexmedetomidine?

A  YES
B  NO
C  MAYBE
Impact of ICU Delirium on Clinical Outcomes
Mortality

<table>
<thead>
<tr>
<th>Study (Year)</th>
<th>OR (95% CI)</th>
<th>% Weight</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ely 2004</td>
<td>3.06 (1.22, 7.67)</td>
<td>7.12</td>
</tr>
<tr>
<td>Kishi 1995</td>
<td>0.96 (0.42, 2.16)</td>
<td>8.02</td>
</tr>
<tr>
<td>Lin 2004</td>
<td>3.63 (1.36, 9.75)</td>
<td>6.59</td>
</tr>
<tr>
<td>Lin 2008</td>
<td>4.09 (1.75, 9.55)</td>
<td>7.71</td>
</tr>
<tr>
<td>Ouimet 2007</td>
<td>7.78 (2.68, 22.59)</td>
<td>6.02</td>
</tr>
<tr>
<td>Salluh 2010</td>
<td>3.50 (1.61, 7.60)</td>
<td>8.37</td>
</tr>
<tr>
<td>Shehabi 2010</td>
<td>3.21 (1.75, 5.90)</td>
<td>10.09</td>
</tr>
<tr>
<td>Tomasi 2012</td>
<td>0.92 (0.18, 4.73)</td>
<td>3.31</td>
</tr>
<tr>
<td>Tomasson 2005</td>
<td>3.77 (1.63, 8.75)</td>
<td>7.77</td>
</tr>
<tr>
<td>Van den Boogaard 2010</td>
<td>3.22 (2.23, 4.66)</td>
<td>12.73</td>
</tr>
<tr>
<td>Van den Boogaard 2012</td>
<td>6.27 (4.19, 9.40)</td>
<td>12.35</td>
</tr>
<tr>
<td>Dubois 2001</td>
<td>1.06 (0.40, 2.81)</td>
<td>6.68</td>
</tr>
<tr>
<td>Shi 2010</td>
<td>6.62 (0.76, 57.96)</td>
<td>2.09</td>
</tr>
<tr>
<td>Tsuruta 2010</td>
<td>21.15 (0.98, 458.53)</td>
<td>1.12</td>
</tr>
<tr>
<td>Overall</td>
<td>3.22 (2.30, 4.52)</td>
<td>100.0</td>
</tr>
</tbody>
</table>

Higher Mortality in Non-Delirium

Higher Mortality in Delirium

Zhang Z. Gen Hosp Psychiatry 2013;35:105-111
Length of Stay & Mechanical Ventilation Duration

- **ICU Length of Stay**
  - 10 studies
  - 7.32 (4.65-10.01) days longer if delirium (+)

- **Hospital Length of Stay**
  - 8 studies
  - 6.53 (3.03-10.03) days longer if delirium (+)

- **Mechanical Ventilation Duration**
  - 4 studies
  - 7.22 (5.15-9.29) days longer if delirium (+)

Zhang Z. Gen Hosp Psychiatry 2013;35:105-111
BZD vs. Non-BZD Clinical Data: Delirium Outcomes
MENDS Trial

Median Duration (Days)

- Delirium- & Coma-Free: Dexmedetomidine 7 days, Lorazepam 3 days; p=0.01
- Delirium-Free: Dexmedetomidine 9 days, Lorazepam 7 days; p=0.09
- Coma-Free: Dexmedetomidine 10 days, Lorazepam 8 days; p<0.001

Pandharipande PP. JAMA 2007;298:2644-2653
SEDCOM Study

Daily Delirium Prevalence

- ↑ overall prevalence in BZD compared to DEX groups (76.6% vs. 54%, respectively, p<0.001)
- ↑ mean delirium-free days associated with DEX over BZD (2.5 vs. 1.7, respectively, p=0.02)
MIDEX and PRODEX Trials

CAM-ICU (+) 48-hr

Dexmedetomidine: 11.9%
Midazolam: 13.9%
p = 0.393

Delirium 48-hr

Dexmedetomidine: 7.7%
Midazolam: 7.6%
p = NS

Delirium 45-day

Dexmedetomidine: 7.7%
Midazolam: 10.0%
p = 0.431

CAM-ICU (+) 48-hr

Dexmedetomidine: 9.6%
Propofol: 13.7%
p = 0.231

Delirium 48-hr

Dexmedetomidine: 2.8%
Propofol: 6.9%
p = NS

Delirium 45-day

Dexmedetomidine: 4.9%
Propofol: 9.7%
p = 0.056
## Delirium Prevalence: Meta-Analysis

**Study** | **Weight** | **RR (95%)** | **Risk Ratio**
---|---|---|---
Pandharipande 2007 | 48.2% | 0.96 (0.79-1.16) | M-H, Random, 95% | Non-Benzodiazepine | Benzodiazepine
Riker 2009 | 51.8% | 0.71 (0.61-0.83) | 0.01 | 101 | 100
Total | 100.0% | 0.82 (0.61-1.11) | 1
Corticosteroids & Delirium Risk

- Prospective cohort study
- n=330 ICU patients with acute lung injury
- Primary outcome: evaluate systemic corticosteroids and other known risk factors for developing ICU delirium

<table>
<thead>
<tr>
<th>Variable</th>
<th>Odds Ratio (95% CI)*</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age 40-60 years</td>
<td>1.81 (1.26 – 2.62)</td>
<td>0.002</td>
</tr>
<tr>
<td>Age &gt;60 years</td>
<td>2.52 (1.65 – 3.87)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Corticosteroid administration</td>
<td>1.52 (1.05 – 2.21)</td>
<td>0.03</td>
</tr>
<tr>
<td>Benzodiazepine administration</td>
<td>1.32 (0.93 – 1.89)</td>
<td>0.12</td>
</tr>
</tbody>
</table>

*Multivariable analysis

Schreiber MP. Crit Care Med 2014;42:1480-1486
BZD-associated Delirium in ICU

- Observational, single-center, cohort study
- n=1112 (mixed med-surg ICU)
- Outcome = awake, no delirium → delirium

<table>
<thead>
<tr>
<th>Variable</th>
<th>Adjusted Odds Ratio* (95% CI)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>BZD Exposure</td>
<td>1.04 (1.02 – 1.05)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>BZD Exposure – Bolus</td>
<td>0.97 (0.88 – 1.05)</td>
<td>0.44</td>
</tr>
<tr>
<td>BZD Exposure – Continuous Infusion</td>
<td>1.04 (1.03 – 1.06)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

*Data represents odds ratio for every midazolam 5mg equivalent
- Outcome = Coma → delirium
- No significant difference on BZD exposure or route of administration
Putting It All Together
## Systematic Review of ICU Delirium Risk Factors

<table>
<thead>
<tr>
<th>Variable</th>
<th>Multivariable Analysis</th>
<th>Univariable Analysis</th>
<th>Level of Evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>High Quality</td>
<td>Positive</td>
<td>Negative</td>
</tr>
<tr>
<td>Analgesodatives</td>
<td>-</td>
<td>2</td>
<td>-</td>
</tr>
<tr>
<td>Benzodiazepines</td>
<td>7</td>
<td>-</td>
<td>1</td>
</tr>
<tr>
<td>Epidural analgesia</td>
<td>1</td>
<td>-</td>
<td>1</td>
</tr>
<tr>
<td>Opiates</td>
<td>3</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Propofol</td>
<td>1</td>
<td>1</td>
<td>-</td>
</tr>
</tbody>
</table>

*Data represents # of studies published for each category

Zaal IJ. Crit Care Med 2015;43:40-47
So What’s The Verdict??

What we know...
- Trials suggesting association vs. no association are balanced
- Delirium assessment may not capture all episodes
- Benzodiazepine agent and regimens varied

What we don’t know...
- Why lower ICU delirium rates in individual trials have not resulted in improved outcomes?
- Lack of overall understanding?
- Are we looking at all variables?
Patient Case Revisited: Midazolam the primary ICU delirium Cause?

- 65 y.o. male
- MSSA sepsis with PNA 5
- PMHx: heroin IVDA
- ARDS
- ECMO
- CAM-ICU (+) w RASS -3

Sedation/Analgesics exposure
- Propofol
- Fentanyl
- Midazolam

A. YES – midazolam is the cause
B. NO – midazolam is NOT the source
C. MAYBE – midazolam could be playing a role, but not clear
Key Takeaways

- **Key Takeaway #1**
  - Conclusive evidence associating BZDs with increased risk of ICU delirium remains controversial

- **Key Takeaway #2**
  - Avoidance of BZD should be based on pharmacokinetic parameters impact on MV duration and ICU length of stay

- **Key Takeaway #3**
  - Be vigilant of all potential modifiable risk factors rather than “tunnel vision” on BZDs
Do Positive CAM-ICU Assessments Identify Delirium in Sedated Patients?

Gil Fraser, PharmD, MCCM
Professor of Medicine, Tufts
Clinical Pharmacist in Critical Care, Maine Medical Center
Objectives

• To provide a balanced view of the limitations of delirium assessment
• To accurately describe the influence of sedation on delirium assessments and associated outcomes
• To identify potential areas for further research
Start With What Is Indisputable

- The brain is a vital organ!
- PAD guidelines recommend non-benzo-based sedation
  - Benzodiazepines prolong time on mechanical ventilation (~2 days) and in the ICU (~1.6 days).
    Fraser CCM 2013; 41:S30
- Sedation-related delirium was the most contentious topic
  - Page 287. “the benzodiazepines MAY BE a risk factor for the development of delirium.” Barr. CCM 2013; 41:263
Start With What Is Indisputable

- Let me administer (in a virtual fashion of course) 5 mg midazolam IV to each of you!!!
Will Almost All of You Be Assessed as CAM-ICU Positive?

A  TRUE

B  FALSE
Confusion-Assessment Method for ICU (CAM-ICU)

Feature 1
Acute Onset of Changes or Fluctuation in Mental Status Course

AND

Feature 2
Inattention

Feature 3
Disorganized Thought

OR

Feature 4
Altered Level of Consciousness

Delirium
The CAM-ICU Can Discriminate Between Pharmacology and Physiology (Delirium)

A  TRUE
B  FALSE
Fake or Real?
Fake or Real?
ICU Delirium

- Frequency: ~50% of ICU patients
- Three-fold increase in 6-month mortality
- An extra 5 days on mechanical ventilation
- An extra 8-10 days of hospitalization costing an average of $15,000/pt
- 50% have cognitive impairment at hospital discharge
  - Long-term in 1/3
- Is sedation use a modifiable risk factor?

Ely. JAMA 2004;291-1753-1762
Milbrandt. CCM 2004;32:955-962
Dubois. ICM 2001; 27:1297
Jones. ICU 2007; 33:978
Finished product
Rock Walls vs Delirium Assessment with CAM-ICU
To Fully Understand, You Need to Dissect
Which of the Following Combinations Are True

A. Benzodiazepine use causes delirium and increases ICU LOS
B. Delirium causes an increase in mortality and is distressing to patients and families
C. Assessing delirium improves outcomes and is easy to do
D. ICU delirium is common but limiting its burden has not been shown to affect outcomes
Delirium and Death

- Delirium experts use words like predict, portend, harbinger of poor outcomes, prognostic indicator, independent risk factor
  - They never use the term “cause”
- If death was causally related to delirium...
  - Limiting its burden would influence survival
  - But it doesn’t!
    - 17 interventional trials with 2800 patients
    - Interventions decreased delirium duration by 64%
    - No effect on short-term mortality; p = .11
- Recent prospective cohort trials could not establish a relationship between delirium and death
  - 1110 patients followed prospectively
  - Delirium prolonged ICU stay, with a 0.9% attributable mortality

Deconstructing and Reconstructing: Some Delirium Questions

- What are the direct consequences of delirium? Death, LTCI, PTSD, distress?

- Does assessing delirium matter? Def, maybe, not one bit!

- How good are our delirium assessment tools? Good, bad, or indifferent? Is there artifact in EVERY measurement we take?

- *Is delirium really a homogeneous dichotomous condition (unlike every other organ failure condition)?*

- **Have we oversimplified a very complex issue?**
  
  *Fraser CCM 2015; 43:703*
Richmond Agitation-Sedation Scale (RASS)

<table>
<thead>
<tr>
<th>Score</th>
<th>Term</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>+4</td>
<td>Combative</td>
<td>Overtly combative or violent; immediate danger to staff</td>
</tr>
<tr>
<td>+3</td>
<td>Very agitation</td>
<td>Pulls on or removes tube(s) or catheter(s) or has aggressive behavior toward staff</td>
</tr>
<tr>
<td>+2</td>
<td>Agitated</td>
<td>Frequent nonpurposeful movement or patient–ventilator dyssynchrony</td>
</tr>
<tr>
<td>+1</td>
<td>Restless</td>
<td>Anxious or apprehensive but movements not aggressive or vigorous</td>
</tr>
<tr>
<td>0</td>
<td>Alert and calm</td>
<td>Not fully alert, but has sustained (more than 10 seconds) awakening, with eye contact, to voice</td>
</tr>
<tr>
<td>−1</td>
<td>Drowsy</td>
<td></td>
</tr>
<tr>
<td>−2</td>
<td>Light sedation</td>
<td>Briefly (less than 10 seconds) awakens with eye contact to voice</td>
</tr>
<tr>
<td>−3</td>
<td>Moderate sedation</td>
<td>Any movement (but no eye contact) to voice</td>
</tr>
<tr>
<td>−4</td>
<td>Deep sedation</td>
<td>No response to voice, but any movement to physical stimulation</td>
</tr>
<tr>
<td>−5</td>
<td>Unarousable</td>
<td>No response to voice or physical stimulation</td>
</tr>
</tbody>
</table>
Does RASS -3 Actually Represent Moderate Sedation?
Per Vanderbilt Authors and Others

Coma  Andresen. CCM 2014; 42:2244, Page Lancet Respir 2013; Sep; 1:515
Severe brain dysfunction  Vasilevskis. CCM 2016; 44:138

And why is this important?

- Coma = ~30-50% increase in time on mechanical ventilation and in the ICU and a 67% increase in neurodiagnostic testing
- Implications for DELIRIUM assessment are huge
  - RASS -3 as a threshold for delirium screening with CAM-ICU either
    - Introduces quite a bit of artifact....OR....
    - Yields a high proportion (91%) of patients who are unable to assess (UTA); Svenningsen 2013; 57:288 (personal communication)
## Prevalence of Delirium is a Function of Wakefulness

<table>
<thead>
<tr>
<th>Prevalence CAM-ICU positive (%)</th>
<th>Sedated</th>
<th>Wakeful</th>
<th>Absolute Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Riker</td>
<td>45-75</td>
<td>12</td>
<td>30</td>
</tr>
<tr>
<td>Ely</td>
<td>83</td>
<td>40</td>
<td>43</td>
</tr>
<tr>
<td>Haenggi</td>
<td>53</td>
<td>31</td>
<td>22</td>
</tr>
<tr>
<td>Poston</td>
<td>73</td>
<td>49</td>
<td>24</td>
</tr>
<tr>
<td>Gusmao-Flores</td>
<td>89</td>
<td>32</td>
<td>57</td>
</tr>
<tr>
<td>Svenningsen</td>
<td>66</td>
<td>22</td>
<td>44</td>
</tr>
<tr>
<td>Patel</td>
<td>77</td>
<td>22</td>
<td>55</td>
</tr>
</tbody>
</table>

22-57% of delirium disappears when patients are wakeful

Riker. CCM 2012; 40:1092  
Ely. JAMA 2001; 286:2703  
Haenggi. ICM 2013; 39:2171  
Posten. AJRCCM 2010:A6701  
Gusmao-Flores ICM 2014; 41:137  
Patel. AJRCCM 2014; 189:658
### RASS and CAM-ICU ASSESSMENTS

**N = 12,875**

<table>
<thead>
<tr>
<th>Study</th>
<th><strong>RASS -2 to -3</strong></th>
<th></th>
<th><strong>RASS 0 to -1</strong></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td># Assessment s</td>
<td># CAM ICU pos</td>
<td>Frequency (%)</td>
<td># Assessment s</td>
</tr>
<tr>
<td>1</td>
<td>588</td>
<td>387</td>
<td>66</td>
<td>9441</td>
</tr>
<tr>
<td>2</td>
<td>92</td>
<td>90</td>
<td>98</td>
<td>71</td>
</tr>
<tr>
<td>3</td>
<td>50</td>
<td>40</td>
<td>80</td>
<td>896</td>
</tr>
<tr>
<td>4</td>
<td>218</td>
<td>212</td>
<td>97</td>
<td>1019</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>948</strong></td>
<td><strong>729</strong></td>
<td><strong>77</strong></td>
<td><strong>11427</strong></td>
</tr>
</tbody>
</table>

Should I do a CAM-ICU assessment before, during, or after a Spontaneous Awakening Trial (SAT)?

“The best picture of the patient’s mental status will come from assessing delirium serially throughout the day. Thus, we recommend that you assess patients for delirium both before and after daily sedative interruption (SAT).”

icudelirium.org accessed 8.15.16

“Drug induced sedation does not, in our opinion, constitute delirium”  Ouimet ICM 2007; 33:66
N = 102 pts: Blinded paired CAM-ICU results before and after daily sedation interruption with one year follow-up

Sedation-related delirium = CAM POS $\rightarrow$ CAM NEG within 2h sedation interruption

10 = no delirium; 12 rapid reversible delirium; 51 persistent delirium; 24 mixed
### Outcomes: No Delirium (ND), Rapidly Reversible Delirium (RRD), Persistent Delirium (PD)

<table>
<thead>
<tr>
<th></th>
<th>ND</th>
<th>RRD</th>
<th>PD</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>ICU LOS (d)</strong></td>
<td>4</td>
<td>4.5</td>
<td>13.1</td>
</tr>
<tr>
<td><strong>Hosp LOS (d)</strong></td>
<td>8.1</td>
<td>6.7</td>
<td>25.4</td>
</tr>
<tr>
<td><strong>MV time (d)</strong></td>
<td>2.4</td>
<td>2.5</td>
<td>6.2</td>
</tr>
<tr>
<td><strong>D/C home (%)</strong></td>
<td>80</td>
<td>100</td>
<td>27</td>
</tr>
<tr>
<td><strong>Mortality % (1yr)</strong></td>
<td>20</td>
<td>25</td>
<td>66</td>
</tr>
</tbody>
</table>

Sedation-related delirium may portend no long-term consequences other than those directly related to their pharmacology (time on the ventilator and in the ICU)
Sedation-Related Delirium

These results clearly demonstrate that the impact of sedation on assessment of delirium cannot be ignored. It may even be questioned whether “rapidly reversible, sedation-related delirium” is delirium at all.

Takala AJRCCM 2014; 189: 622

Unfortunately, almost all ICU delirium research has been done without considering the role of sedation at all and therefore appears to be seriously flawed. Takala AJRCCM 2014; 189:1444
Wakefulness and Delirium Assessment

- Delirium assessments AND outcomes are influenced by depth of sedation

Implication

- Assess sedated patients after they have exhibited wakefulness (SAS 3-4 or RASS 0 to -2 with additional commands)
Key Takeaways

• Delirium assessment with CAM-ICU is best performed when patients are wakeful
• It is not likely that sedative-associated positive CAM-ICU assessments have any impact beyond pharmacologic interference with ventilator weaning and ICU discharge
• We need to
  o Develop accurate definitions of ICU delirium
  o Discover meaningful aspects of ICU delirium
  o Find modifiable risk factors that are real and relevant
“It doesn't take a chef to know the milk is spoiled.” G Fraser 2013
Easy as 123: ABCDEF Bundle Implementation and Performance Assessment

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Objective

- Recommend implementation strategies for sedation, delirium, and mobility for best practices in ICU patients.
Key Concept: ABCDEF Bundle

A • Assess, Prevent, and Manage Pain

B • Both Spontaneous Awakening (SATs) & Spontaneous Breathing Trials (SBTs)

C • Choice of Analgesia & Sedatives

D • Delirium Reduction, Assessment, and Management

E • Early Mobility & Exercise

F • Family Engagement and Empowerment
Audience Survey:

Do you feel your institution has robust ABCDEF bundle processes in place?

A  YES
B  NO
Basic Approach: ABCDEF Bundle

- **Assess, prevent, and manage pain**
  - Pain assessment is key to adequate pain control
  - Pain before sedation

- **Both spontaneous awakening and breathing trials**
  - Daily sedation interruption or light sedation levels

- **Choice of sedation and analgesia**
  - Non-benzodiazepine sedative agents recommended (propofol or dexmedetomidine) in mechanically ventilated patients

Basic Approach: ABCDEF Bundle

- **Delirium assessment, prevention, and management**
  - Daily screening tools to assess for delirium
  - Address modifiable risk factors and non-pharmacological interventions
  - Discontinue potential deliriogenic medications
  - Haloperidol or atypical antipsychotics may be used

- **Early mobility and exercise**
  - Early mobilization helps with muscle strength, delirium, and functional status

- **Family Communication**
  - Ongoing dialogue with family about care and involving family in the decision making

Summary of Benefits: ABCDEF Bundle

- Decreased ventilator time
- Decreased ICU length of stay
- Improved return to normal mental status
- Increased independent functional status
- Improved patient and family satisfaction
- Improved mortality

Tools & Resources

- Society of Critical Care Medicine’s (SCCM) ICU Liberation Campaign
  - [http://www.iculiberation.org/Bundles/Pages/default.aspx](http://www.iculiberation.org/Bundles/Pages/default.aspx)

- American Association of Critical Care Nurses (AACN) Implementing ABCDE Bundle at the Bedside
Tools & Resources

- Baylor Research Institute and the Society of Hospital Medicine

- Vanderbilt University Medical Center, Center for Health Services Research
  - [http://www.icudelirium.org/medicalprofessionals.html](http://www.icudelirium.org/medicalprofessionals.html)
Step-by-Step

- **STEP 1:** Identify ICU champion(s)
  - Nurse, physician, pharmacist or quality specialist
- **STEP 2:** Create the committee to develop and guide processes
- **STEP 3:** Highlight current practices and perform gap analysis
  - What are we doing well?
  - What are the opportunities for improvement?

Step-by-Step

- **STEP 4:** Develop and implement bundle processes
  - Toolkits, scripts, flowsheets
  - Encourage and enable staff contributions
- **STEP 5:** Deploy interventions and educate staff
  - Integrated within daily workflow
- **STEP 6:** Collect data and report on specific measures
  - Disseminate findings among staff
- **STEP 7:** Celebrate the successes and continue to evolve

Inter-disciplinary Effort

Patient & Family

- Pharmacists
- Nurses
- Physicians
- Respiratory Therapy
- Physical Therapy/ Rehab
## Role of Pharmacists & Team Members

<table>
<thead>
<tr>
<th>Bundle Element</th>
<th>Primary Accountability</th>
<th>Additional Team Member Responsibility</th>
</tr>
</thead>
<tbody>
<tr>
<td>A Assess, Manage and Treat Pain</td>
<td>RN</td>
<td>MD, Pharm</td>
</tr>
<tr>
<td>B Both Awakening and Breathing</td>
<td>RN, RT</td>
<td>RN, MD, Pharm</td>
</tr>
<tr>
<td>C Choice of Analgesia and Sedation</td>
<td>RN</td>
<td>RT, MD, Pharm</td>
</tr>
<tr>
<td>D Delirium Assessment, Prevention, Management</td>
<td>RN</td>
<td>RT, Pharm, MD, PT</td>
</tr>
<tr>
<td>E Early Mobility and Exercise</td>
<td>RN, PT</td>
<td>RT</td>
</tr>
<tr>
<td>(F) Family Engagement</td>
<td>RN</td>
<td>All</td>
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Assess, Manage and Treat Pain

- Use Behavioral Pain Scale (BPS) or Critical-Care Pain Observance Tool (CPOT)
- Routinely monitored
- Potential goals:
  - Assess pain four or more times per shift
  - Treat pain within 30 minutes of detecting significant pain, then reassess
- Preemptive analgesia for potentially painful procedures
- Treat pain first, then sedate

TGH Experience: Pain

- Gap Analysis:
  - Pain scoring well integrated into practice in all ICUs
    - HCAHPs score focus & education
    - Routine engagement and direct feedback
  - The next frontier = analgosedation!
    - Focus on analgesics for pain and sedation → reduction in sedative usage other potential benefits
    - Despite potential advantages, analgosedation practiced inconsistently throughout ICUs
    - Opportunities for further adoption
TGH Experience: Analgosedation

- Ongoing study: mechanically ventilated Medical ICU patients
  - Prospective, randomized, single center
  - Patients randomized in a 1:1 fashion to one of two groups:
    - Group 1: new analgosedation protocol
      - Nurse driven
      - Fentanyl infusion + midazolam bolus dosing PRN
    - Group 2: standard of care
      - Provider driven without protocol
        - Continuous infusion sedative usage common practice
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SATs & SBTs

- Wake Up & Breathe Protocol
  - Vanderbilt University
  - Performed daily
  - Patients who fail screening or trial, returned to targeted sedation protocol and/or ventilator support
- Requires true collaboration

Vanderbilt University Medical Center. Wake Up and Breathe protocol; 2008.
TGH Experience: SATs & SBTs

- Gap Analysis:
  - Evolving practice
  - Shifting to patient-centered versus “protecting our territories”
  - CTICU leading effort
  - Other ICUs following suit
  - Protocol in place

- Stage 1: Screen criteria for initiation of protocol
- Stage 2: Assess for exclusions
- Stage 3: Wean FIO2
- Stage 4: Wean PEEP
- Stage 5: Wean respiratory rate
- Stage 6: Change mode to pressure support ventilation
- Stage 7: Weaning parameters
- Stage 8: Extubation

Fraction Inspired Oxygen (FIO2); Positive End Expiration Pressure (PEEP)
Key Concept: ABCDE Bundle

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Choice of Sedation

- Targeted Sedation Protocols
  - Non-benzodiazepine sedatives preferred
- Targeting sedation goals
  - Maintain light rather than deep sedation
    - Riker Sedation Agitation Scale (SAS)
    - Richmond Agitation Sedation Scale (RASS)
- Minimizes drug exposure and accumulation
- Optimizes patient alertness

TGH Experience: Choice of Sedation

- **Gap Analysis**
  - Guidelines in place
  - Previous challenges with lack of sedation assessment (<20% compliance with RASS pre-intervention)
    - Extensive nursing education performed & electronic medical record (EMR) documentation pathway optimized
      - >95% compliance with RASS post-intervention!!
  - “Sedation Stewardship” encouraged (similar to Antimicrobial Stewardship)
    - Indication
    - Drug choice
    - Duration/de-escalation
    - Outcomes/reactions
      - Delirium
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TGH Experience: Delirium

- Gap Analysis:
  - Over a decade of effort
  - Making progress

March 2006 Delirium Task Force Formed: CAM-ICU instituted
Oct 2011 EPIC EMR Go-Live
Aug 2012 Early Mobility Protocol instituted

Confusion Assessment Method-ICU (CAM-ICU); Intensive Care Delirium Screening Checklist (ICDSC)
TGH Experience: Making Progress

- Apr 2013: ICDSC, & RASS Flowsheet rows in EPIC
- May 2013: Pharmacy Delirium Assess: workbench report
- Nov 2014: Delirium Committee formed: Nursing Quality
- May 2016: Delirium Screen in EPIC Patient Scoring
- Sept 2016: ICU Liberation Team Coaching in ICU
TGH Experience: Role of ICU Pharmacists

- Patients identified with ICDSC score ≥ 4 in EMR (i.e., EPIC)
  - Report run daily (i.e., EPIC workbench report) → Evolved to automatic flag in patient list (i.e., EPIC scoring)
- Delirium treatment guidelines
- Review medication list for deliriogenic medications
- Ensure non-pharmacologic delirium prevention utilized
- Call provider if necessary
- Document recommendations/interventions in a progress note
  - Use smart phrase template: .RPHDELIRIUM

>95% Compliance with pharmacy delirium assessments

Additional outcome measures being considered
Key Concept: ABCDEF Bundle

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Early Mobility

- Preventative physical and cognitive rehabilitation
- Engages the critically ill
- Activities help in recovery
- Prevents muscle deterioration and joint contractures
- Requires a proactive approach

TGH Experience: Early Mobility

- **Gap Analysis:**
  - Prior leaders (e.g., Surgery/Trauma ICU, Neuro ICU)
  - Recently expanded nurse protocol for all ICUs

- **Not on bedrest, RN screens (using the MOVE criteria):**

  | M | Myocardial Stability | No evidence of myocardial ischemia in 24 hours |
  | O | Oxygenation Adequacy | FIO2 <0.6 and PEEP <10 |
  | V | Vasopressors | SBP stable at >90 or at baseline.
  | E | Engagement to Voice | If vasoactive, minimal dose or no increase in 2 hrs |
  |   | Responds to verbal stimuli. ICP < 20 |

Intracranial Pressure (ICP)
Key Concept: ABCDEF Bundle

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F • Family Engagement and Empowerment
Family

- Keep ICU patients and families informed
- Encourage active patient and family involvement in decision making
  - Help provide physical comfort and emotional support
- Rounding
  - ICU Liberation videos
TGH Experience: Family

- Gap Analysis:
  - Family engaged during rounding by physicians primarily, and as needed
  - Opportunities for additional family engagement from the larger interdisciplinary team
  - Lack of clear and consistent roles for family interactions

- ICU Liberation project underway
  - Evaluating options for optimizing rounding
    - Pharmacist/Team script being evaluated for feasibility
      - Pain
      - Sedation
      - Delirium
Challenges

- Awareness: What is ABCDEF Bundle?
- Buy-in: How does this benefit our department/discipline/institution?
- Practice area differences: How do we align practices across ICU settings?
- Process: How do we (department/discipline/institution) implement?
  - Should this be unit-specific or housewide?
- Sustainability/scalability: Will we be able to maintain progress, or make further gains?
- Impact: Are we truly making an impact?
Metrics to Consider: Process Measures

- Pain score compliance
  - % of patients assessed for pain (BPS, CPOT)
- Sedation score compliance
  - % of patients assessed for sedation (RASS or SAS)
- Delirium score compliance
  - % of patients screened for delirium (CAM-ICU or ICDSC)
- SAT & SBT compliance
  - % of patients contraindicated for SAT
  - % of patients received SBT
- Early mobility compliance
  - % of patients early mobilized (active or passive?)
- Delirium assessment compliance
  - % delirium assessments completed
Metrics to Consider: Outcome Measures

- Mechanical ventilator days
- ICU length of stay
- Delirium diagnosis rates
- Delirium response
  - % delirious patient response within encounter?
Question:

Which of the following is a potential benefit of ABCDEF bundle implementation?

A. Decreased ICU length of stay
B. Improved return to normal mental status
C. Decreased ventilator time
D. All of the above
Key Takeaways

- **Key Takeaway #1**
  - Implementation of ABCDEF bundle processes require initial staff awareness of benefits to patients, followed by identification of ICU champion(s).

- **Key Takeaway #2**
  - A gap analysis should be performed for A-B-C-D-E-F, in order to understand current state and opportunities.

- **Key Takeaway #3**
  - SCCM ICU Liberation Campaign, and AACN ABCDE Bundle at the Bedside provide excellent resources (e.g. toolkits, scripts, videos, flowsheets, etc) to aid in implementation.