CSHP SEMINAR 2016
TRANSITIONS
IN PHARMACY
DISNEYLAND® RESORT • OCTOBER 27th – 30th
ICU Liberation for the Pharmacist

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Disclosure

No conflicts of interest to disclose
Objectives

- Outline the elements of the ABCDEF bundle and the evidence behind their recommendations
- Examine the impact of delirium on morbidity and mortality in ICU patients
- Describe the role of the critical care pharmacist in optimizing pain, agitation, and delirium management as part of the interprofessional ICU team
A Paradigm Shift

- 2002 Society of Critical Care Medicine Guidelines
  Clinical practice guidelines for the sustained use of sedatives and analgesics in the critically ill adult

- 2013 Society of Critical Care Medicine Guidelines
  Clinical Practice Guidelines for the Management of Pain, Agitation, and Delirium in Adult Patients in the Intensive Care Unit

ICU Liberation: It's As Easy As...

A. Assess, Prevent, and Manage Pain
B. Both Spontaneous Awakening and Breathing Trials
C. Choice of Sedative and Analgesic Medications
D. Delirium Monitoring and Management
E. Early Mobilization and Exercise
F. Family Engagement and Empowerment
Is it that easy?

- Implementation of ABCDE bundle
  - Single center, pre/post study (n= 296)
  - Lower delirium prevalence (62% vs 49%, p=0.02)
  - Fewer days in delirium (33.3% vs 50%, p=0.003)
  - More ventilator free days (21 vs 24 days, p=0.04)
  - Increased mobilization (66% vs 48%, p=0.002)
(A)nalgesia
Assess, Prevent and Manage Pain
Assess, Prevent and Manage Pain

- Assess pain routinely
- Consequences of untreated pain
- Choice of analgesic

Guidelines: we suggest that analgesia-first sedation be used in mechanically ventilated adult ICU patients (+2B).
- Pain frequently causes agitation
- Limited comparative data (~4 studies)

Analgosedation at UCSF

Patients prescribed continuous sedation (n=22)
- MSICU
- 30-day audit

Compared analgesic use pre/post sedation

<table>
<thead>
<tr>
<th>Sedative Timeframe</th>
<th>Received IV Opioid, n (%)</th>
<th>Mean Opioid Doses</th>
</tr>
</thead>
<tbody>
<tr>
<td>6 Hours Prior</td>
<td>12 (55%)</td>
<td>89 mcg&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>Hours 0 - 6</td>
<td>11 (50%)</td>
<td>59 mcg&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>Hours 7 - 12</td>
<td>10 (45%)</td>
<td>55 mcg&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>Hours 13 - 18</td>
<td>8 (36%)</td>
<td>37 mcg&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>Hours 19 - 24</td>
<td>5 (23%)</td>
<td>15 mcg&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

<sup>a</sup> mcg fentanyl equivalents
<sup>b</sup> mg oxycodone equivalents
(B)reathing
Both Spontaneous Awakening and Breathing Trials
Guideline Recommendations

- Recommend *either daily sedation interruption or light target level of sedation* be routinely used in mechanically ventilated ICU patients (+1B)

- Maintaining light levels of sedation in adult ICU patients is associated with *improved clinical outcomes* (B)

- Recommend that sedative medications be titrated to maintain a light rather than a deep level of sedation, *unless clinically contraindicated* (+1B)

Spontaneous Awakening and Breathing Trials

Daily awakenings trial (n=128)
- Daily spontaneous awakening trial (SAT)
- Fewer ventilator days, shorter ICU LOS

ABC trial (n=336)
- Paired SAT + spontaneous breathing trial (SBT)
- Fewer ventilator days, shorter ICU/hospital LOS, lower 1 year mortality, less delirium/coma

Protocolized sedation (n=430)
- Protocolized sedation + SAT + SBT vs. protocolized sedation
- No difference in ventilator days, LOS, delirium + increased workload
- Included benzodiazepines and opioids only
SAT/SBT: The Pharmacist’s Role

Single center MICU QI study (n=1,296 MV days)
  ◦ Pre, during, post QI periods

Intervention
  ◦ Pharmacist led education
  ◦ Daily discussion on rounds
  ◦ Weekly performance reports to staff

Results
  ◦ Increased SAT screening and completion rates
  ◦ Increased number of passed SATs
  ◦ Similar days with sedative/analgesic infusions

# Targeting Light Sedation: 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, violent, immediate danger to staff</td>
</tr>
<tr>
<td>+3</td>
<td>Very agitated</td>
<td>Pulls or removes tube(s) or catheter(s); 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 but movements not aggressive vigorous</td>
</tr>
<tr>
<td>0</td>
<td>Alert and calm</td>
<td>Not fully alert, but has sustained awakening</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(eye-opening/eye contact) to voice (<strong>10 seconds</strong>)</td>
</tr>
<tr>
<td>-1</td>
<td>Drowsy</td>
<td>Briefly awakens with eye contact to voice (<strong>10 seconds</strong>)</td>
</tr>
<tr>
<td>-2</td>
<td>Light sedation</td>
<td>Movement or eye opening to voice (<strong>but no eye contact</strong>)</td>
</tr>
<tr>
<td>-3</td>
<td>Moderate sedation</td>
<td>No response to voice, but movement or eye opening</td>
</tr>
<tr>
<td></td>
<td></td>
<td>to physical stimulation</td>
</tr>
<tr>
<td>-4</td>
<td>Deep sedation</td>
<td>No response to voice or physical stimulation</td>
</tr>
<tr>
<td>-5</td>
<td>Unarousable</td>
<td>No response to voice or physical stimulation</td>
</tr>
</tbody>
</table>

**Verbal Stimulation**

**Physical Stimulation**

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Target RASS Score Optimization

What?

◦ Relocated target RASS from sedative order admin instructions to separate order
◦ Integrated into ICU rounds structure

Why?

◦ To ensure target RASS set for all patients
◦ To improve early recognition of (hypoactive) delirium
◦ To improve consistency between orders
◦ To increase visibility to clinicians

ICU Liberation
(C)hoice
Choice of Analgesic and Sedative Medications
Can mechanically ventilated patients be managed without sedation?

A protocol of no sedation for critically ill patients receiving mechanical ventilation: a randomised trial

Thomas Strøm, Torben Martinussen, Palle Toft

Lancet 2010; 375: 475–80
No Sedation?

Prospective, open-label; mechanically ventilated patients
- Morphine PRN
- Morphine PRN + propofol/midazolam + SAT

Results (n=140)
- No sedation is feasible (18% didn’t tolerate)
- ↓ mechanical ventilation days, ICU/hospital LOS
- No difference in PTSD (follow-up study)
- Post-hoc analysis
  - ↑ Hyperactive delirium
  - ↓ Acute renal failure

Benzodiazepines and Delirium Risk!

Single center, prospective cohort (n=275)
- Mechanically ventilated patients

Lorazepam
- Independent risk factor for transitioning to delirium
- OR 1.2 (95% CI 1.1-1.4), p=0.003
Benzodiazepines and Delirium Risk?

Mixed ICU (n=1,112)
- 9,867 daily transitions
- Light sedation, SAT, CAM-ICU screenings

BZD and delirium risk
- Awake patient without delirium given BZD
- ↑ risk of delirium next day (OR 1.04)
- Association with BZD infusion only

Mixed ICUs (n=1,235)
- BZD vs. propofol or dexemedetomidine

Non-BZD sedation:
- Shorter ICU LOS (1.62d)
- Shorter MV (1.9d)
- Similar delirium prevalence (RR 0.83, 95% CI 0.61-1.11)
- Similar short term mortality
MENDS Trial

DBRCT (n=106)
- Mechanically ventilated ICU patients (> 24h)

Primary Outcomes
- Delirium/coma free days
- Time at sedation goals

Secondary Outcomes
- ICU LOS
- Mortality

SEDCOM Trial

DBRCT (n=375)
- Mechanically ventilated (> 24h)

Primary Outcome
- Time at sedation goal

Secondary Outcomes
- Delirium prevalence, duration

Figure 2. Daily Prevalence of Delirium Among Intubated Intensive Care Unit Patients Treated With Dexmedetomidine vs Midazolam

PRODEX/MIDEX Trials

Parallel DBRCTs (MIDEX n=500, PRODEX n=498)
- Mechanically ventilated ICU patients (sedation >24 hours)
- Time at sedation target (noninferiority)
- Ventilation days (superiority)

Guidelines: Choice of Sedative

- **Non-benzodiazepines** (propofol or dexmedetomidine) are preferred (+2B)

- Dexmedetomidine sedation may be associated with a **lower delirium prevalence** than benzodiazepines in patients at risk for delirium (B)

- **No recommendation** for dexmedetomidine to **prevent** delirium (no evidence, C)
(D)elirium
Monitoring and Management
ICU Delirium: Scope of the Problem

Incidence
- 60-80% of mechanically ventilated patients
- Up to 60% of lower acuity ICU patients

Impact
- Independent predictor of mortality
- Long term cognitive dysfunction
- Poor functional status
- Duration of mechanical ventilation, reintubation rates
- Increases hospital/ICU length of stay
- Increased healthcare costs

References:
- Pandharipande PP. NEJM 2013;369:1306-16.
- AJRCCM 2009 12; 180(11): 1092–1097
ICU Survivors and Cognitive Impairment

Normal
Mild impairment
TBI
Alzheimer’s

Figure 1. Global Cognition Scores in Survivors of Critical Illness.

Paripanpande PP et al. NEJM 2013;369:1306-16.
ICU Delirium and Cognitive Impairment

More \textit{days} \textit{with} delirium associated with poorer global cognition scores

Figure 2. Duration of Delirium and Global Cognition Score at 12 Months.
Delirium Monitoring

- Can be unrecognized in 66-84% of hospitalized adults
- Regular screening with a validated tool is imperative

References:
Delirium Subtypes

![Graph showing delirium subtypes](image-url)

- **All Delirium**
- **Hypoactive**
- **Mixed**
- **Hyperactive**

Percent of Patients in Age Category

- 65 Years and Older (N=155)
- Younger than 65 (N=459)

Delirium Subtype during Medical Intensive Care Unit Admission

*Chest 2007; 132; 624-636.*
Confusion Assessment Method for the ICU (CAM-ICU) Flowsheet

1. Acute Change or Fluctuating Course of Mental Status:
   - Is there an acute change from mental status baseline? **OR**
   - Has the patient’s mental status fluctuated during the past 24 hours?
   - **YES**

2. Inattention:
   - “Squeeze my hand when I say the letter ‘A’.”
   - Read the following sequence of letters: S A V E A H A A T
   - ERRORS: No squeeze with ‘A’ & Squeeze on letter other than ‘A’
   - If unable to complete Letters → Pictures
   - **NO DELIRIUM**

3. Altered Level of Consciousness
   - Current RASS level
   - RASS = zero
   - **NO DELIRIUM**

4. Disorganized Thinking:
   - Will a stone float on water?
   - Are there fish in the sea?
   - Does one pound weigh more than two?
   - Can you use a hammer to pound a nail?
   - Command: “Hold up this many fingers” (Hold up 2 fingers)
   - “Now do the same thing with the other hand” (Do not demonstrate)
   - **NO DELIRIUM**
   - OR “Add one more finger” (If patient unable to move both arms)
   - **NO DELIRIUM**

CAM-ICU negative

CAM-ICU positive

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#### The Bedside Assessment

<table>
<thead>
<tr>
<th></th>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nurse</td>
<td>CAM: +</td>
<td>31</td>
</tr>
<tr>
<td></td>
<td>CAM: -</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>CAM: NA</td>
<td>1</td>
</tr>
<tr>
<td>Sensitivity</td>
<td>0.35</td>
<td></td>
</tr>
<tr>
<td>Specificity</td>
<td>0.98</td>
<td></td>
</tr>
<tr>
<td>PPV</td>
<td>0.91</td>
<td></td>
</tr>
<tr>
<td>NPV</td>
<td>0.74</td>
<td></td>
</tr>
<tr>
<td>Physician</td>
<td>CAM: +</td>
<td>25</td>
</tr>
<tr>
<td></td>
<td>CAM: -</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>CAM: NA</td>
<td>1</td>
</tr>
<tr>
<td>Sensitivity</td>
<td>0.28</td>
<td></td>
</tr>
<tr>
<td>Specificity</td>
<td>1.00</td>
<td></td>
</tr>
<tr>
<td>PPV</td>
<td>1.00</td>
<td></td>
</tr>
<tr>
<td>NPV</td>
<td>0.73</td>
<td></td>
</tr>
</tbody>
</table>

RN = 35%

Attending = 28%
Antipsychotics for ICU Delirium?

1. Devlin, et al. (n=36); treatment
   - Quetiapine + haloperidol PRN vs. haloperidol PRN
   - ↓ time to first delirium resolution (1 vs. 4.5 days)
   - ↓ duration of delirium (36 vs. 120 hours)
   - ↓ agitation (6 vs. 36 hours)
   - ↓ PRN haloperidol vs. placebo

Quetiapine for Intensive Care Unit Delirium: The Evidence Remains Weak

John W. Devlin,1,2,* Christopher J. Michaud,3 Heather M. Bullard,4 Serena A. Harris,5 and Wendy L. Thomas,3
DahLIA: Dexmedetomidine for Delirium?

Double blind, placebo controlled, randomized parallel group trial
- Extubation inappropriate due to hyperactive delirium (n=72)
- Dexmedetomidine added

Outcomes
- More MV-free hours
- Faster resolution of delirium
- Reduced other sedative/analgesic use

Guidelines: Treatment of Delirium

- There is no published evidence that treatment with haloperidol reduces the duration of delirium in adult ICU patients (No Evidence).

- Atypical antipsychotics may reduce the duration of delirium in adult ICU patients (C).

- We suggest that in adult ICU patients with delirium unrelated to alcohol or BZD withdrawal, IV infusions of dexmedetomidine rather than BZD infusions be administered for sedation to reduce the duration of delirium in these patients.
## Antipsychotics at Transitions of Care

<table>
<thead>
<tr>
<th></th>
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<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>ICU population</td>
<td>Medical ICU (n=59)</td>
<td>Mixed ICUs (n=156)</td>
<td>Mixed ICUs (n=3,119)</td>
</tr>
<tr>
<td>Antipsychotics</td>
<td>Atypical</td>
<td>Atypical</td>
<td>Any Inpatient initiation</td>
</tr>
<tr>
<td></td>
<td>For delirium</td>
<td>At least 2 doses</td>
<td></td>
</tr>
<tr>
<td>Continued at ICU DC?</td>
<td>28/59 (47%)</td>
<td>112/133 (84.2%)</td>
<td>--</td>
</tr>
<tr>
<td>Continued at hospital DC?</td>
<td>20/28 (71%)</td>
<td>38/133 (28.6%)</td>
<td>642/3119 (21%)</td>
</tr>
</tbody>
</table>
Transitions of Care at UCSF

Observational, pre/post study (n=93)

- Quetiapine initiated for ICU delirium
- Implemented electronic intervention + education
  - CPOE medication order with automatic stop

<table>
<thead>
<tr>
<th></th>
<th>Pre (n=66)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Continued on ICU discharge</td>
<td>44.0%</td>
</tr>
<tr>
<td>Continued on hospital discharge</td>
<td>22.7%</td>
</tr>
</tbody>
</table>
### Bundled Intervention for Sleep and Delirium

#### Multifaceted QI intervention (Hopkins MICU)

<table>
<thead>
<tr>
<th>Stage</th>
<th>Intervention</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>Baseline</td>
</tr>
<tr>
<td>1</td>
<td>Stage 1: Environmental interventions</td>
</tr>
<tr>
<td>2</td>
<td>Stage 2: Non-pharm sleep aids</td>
</tr>
<tr>
<td>3</td>
<td>Stage 3: Pharmacologic guideline</td>
</tr>
</tbody>
</table>

#### Baseline Sleep QI vs. Sleep QI

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>Sleep QI</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Delirium/Coma Free days</td>
<td>43%</td>
<td>48%</td>
<td>p=0.04</td>
</tr>
<tr>
<td>Incident Delirium/Coma</td>
<td>69%</td>
<td>49%</td>
<td>p=0.001</td>
</tr>
</tbody>
</table>

No difference: mortality, LOS, neurocognitive tests, perceived sleep quality

Kamdar et al. *Crit Care Med* 2013; 41: 800-809
Ramelteon and Delirium?

Ramelteon vs. placebo in elderly patients (n=67)

Delirium incidence
3% vs. 32%
(p=0.003)

Figure 3. Time to Development of Delirium

Hatta K, et al. JAMA Psychiatry 2014
Summary: Drugs and Delirium

Less is more
- Minimize deliriogenic medications
- Choose appropriate sedation (treat the patient!)

Antipsychotics
- Limited evidence, risk for ADE
- Long term impact and costs unknown
- May reduce duration of delirium

Melatonin agonists
- May be effective for prevention
(E)xercise
Early Mobilization and Exercise
Early Mobilization

Guidelines: Recommend performing early mobilization of adult ICU patients whenever feasible to reduce the incidence and duration of delirium (+1B)

Requires optimizing ICU environment (and culture) for mobility
  ◦ Pain and sedation management
  ◦ Sleep promotion

Early Rehabilitation and Delirium

Schweickert *et al*, 2009

- Progressive algorithm ~1.5 days post-intubation
- Shorter duration of ICU delirium (2 vs. 4 days, p=0.03) with similar sedative administration/SAT

Needham *et al*, 2010

- Reduced benzodiazepines (BZD)
  - Days with bzd (25% vs. 50%, p=0.002)
  - Total daily dose of bzd (47 mg vs. 15 mg, p=NS)
- Reduced delirium (21% vs. 53%, p=0.003)
Single center, observational study (n=327 MICU patients)

Factors influencing “next day” PT participation

- Perceived sleep quality = no association
- Delirium
- Continuous sedative use
- IV opioid bolus requirements
- Benzodiazepines
Family Bundle

Goals
- Improve awareness
- Frame discussions

Patient/family advisory committee input

Disseminated to floor and ICU services
ICU Liberation: It’s as Easy As...

A
- Analgesia
  Use appropriate pain scales (Pain Verbal Scale, NRS, or CPOT)
  Treat pain before sedating

B
- Breathing
  Perform and pair daily SAT & SBT (unless contraindicated)

C
- Choice
  Set and monitor a target RASS & a target pain level decrease
  Avoid benzodiazepines when possible

D
- Delirium
  CAM ICU with each shift assessment & prn
  Promote nighttime sleep
  (noise & lights; earplugs & eyeshades)

E
- Exercise
  Mobilize patients daily
  Consult PT/ST/OT for rehab
  Coordinate lighter sedation with rehab

F
- Family
  Provide family education brochure
  Encourage visits and conversations
  Bring in familiar & essential items from home

ABBREVIATION GLOSSARY
NRS = Numeric Rating Scale
RASS = Richmond Agitation Sedation Scale
CAM-ICU = Confusion Assessment Method for ICU
PT = Physical Therapy
ST/OT = Speech Therapy/Occupational Therapy
The Future? Emerge Harms Monitor

GENDER: M
AGE: 38

FAMILY SPOKESPERSON:
See medical record

SURROGATE:
See medical record

PREFERRED:
NAME:
Patient Users: 0
Family Users: 1

Patient Schedule
Patient Profile
Set Family Activities

Harms Monitor
Alignment Of Goals
Ventilator Associated Events (VAE)
Venous Thromboembolic Events (VTE)
CLABSI
Respect and Dignity
ICU Acquired Weakness (IAW)
Delirium

Last Refresh: 07Mar2016 14:23
It Takes the Whole Team (including Pharmacists)!

- Judicious sedation
- Early rehabilitation
- Maximize delirium screening
- Awake and breathing coordination
- Recognize and treat pain
- Optimize ICU environment
- Consider home and deliriogenic medications

ICU Liberation
Want to learn more?

ICU Liberation (www.iculiberation.org)
  ◦ Maintained by SCCM

ICU Delirium (www.icudelirium.org)
  ◦ Maintained by Vanderbilt University
Assessment Questions

Which of the following is NOT a complication of ICU delirium?

a. Mortality
b. Over-sedation
c. Long-term cognitive dysfunction
d. Increased costs

Pharmacologic therapy is first line for the treatment and prevention of delirium.

a. True
b. False
Session Code:

1. Write down the course code. Space has been provided in the daily program-at-a-glance sections of your program book.

2. To claim credit: Go to www.cshp.org/cpe before December 1, 2016.