Improving the Management of Pain, Agitation, and Delirium (PAD) in the Intensive Care Unit: Translating Evidence Into Practice

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NYS Partnership for Patients

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Objectives

• Apply strategies for operationalizing pain and agitation guidelines into clinical practice

• Select appropriate sedative medications using validated scales for pain, agitation, and delirium in the intensive care unit

• Define the pharmacist’s role in optimizing the management of pain, agitation, and delirium in critically ill patients
University of Rochester Medical Center

850-bed tertiary care hospital

120-bed emergency department (ED)
  • Level 1 trauma
  • Comprehensive stroke center

Adult ICUs (~100 beds)
  • MICU
  • SICU
  • Burn/Trauma ICU
  • Neuro ICU
  • CVICU

Progressive care units
  • MICU, SICU, trauma
Traditional PAD Practices at SMH

**Pain**
- Fentanyl Infusions
- Goal: NVPS <4

**Agitation**
- Benzodiazepine Infusions
- Goal: SAS 3-4
- Sedation Holidays

**Delirium**
- Haloperidol ATC/PRN
- Subjective Assessment

NVPS: Nonverbal Pain Scale
SAS: Riker Sedation-Agitation Scale
Traditional PAD Practices at SMH

Original pain and sedation guideline
- Fentanyl and lorazepam continuous infusions as first-line
- Propofol as second-line agent

Revised pain and agitation guideline (~2007)
- Attempted intermittent sedation first
- Changed to midazolam infusions over lorazepam
- Complicated with multiple algorithms
Traditional PAD Practices at SMH

Trialed an intermittent pain and agitation protocol that failed
- Complexity in implementing without electronic medical record
- Regulations around handling controlled substances

Delirium not addressed
- Treated like an expected occurrence
- Assumed it would resolve with time
Quality Improvement Process for PAD management

- Summarize the evidence
- Identify local barriers
- Measure performance
- Ensure all patients receive the strategy

Engage → Evaluate → Execute → Educate
Ensure all Patients Receive the Strategy

- Explain why interventions are important
- Share evidence supporting interventions
- Assess performance measures and unintended consequences
- Target barriers, standardize care, include checks and reminders, and learn from mistakes

Summarize the Evidence

- **Analgosedation**
  - Assess for pain first
  - Opioids prior to sedatives for agitation

- **Intermittent Sedation**
  - Implement protocol after intubation
  - Use to help wean off infusions

- **Reduce Benzodiazepine Use**
  - Promoting analgosedation
  - Promoting use of non-benzo sedatives

- **Sedation Interruptions**
  - Improve compliance
  - Encourage sedation reductions

- **Delirium Management**
  - Start monitoring with validated tool
  - Develop treatment guideline
Identify Local Barriers

- Lack of awareness that sedative agents can cause harm
- Outdated and complex pain and sedation guideline
- Physician order entry process
- No process for delirium detection and management
  - Choose a tool for monitoring delirium
  - Nursing by-in to monitor for delirium
  - Increase provider awareness
  - Develop a guideline for management
Engaging and Educating Health-care Professionals on the Harm in Oversedation

Sedative medication error patient cases
- Interactive
- Open for discussion

Discussions on patient care rounds
- Point out what we do well
- Point out what we could’ve done better

One-on-one discussions at the bedside

Empowering nurses on their ability to improve patient outcomes

Use of Validated Scales
- Treating pain first
- Trial intermittent sedation first
- Bolus prior to increasing infusions
- Sedation holidays/reductions
**Effect of a Nursing-Implemented Sedation Protocol on the Duration of Mechanical Ventilation**

The protocol:
- Assessed pain first
- Corrected other etiologies for agitation
- Used sedation score to titrate sedatives
- Used intermittent sedation first
- Actively down-titrated sedation even when patient was at “goal”

<table>
<thead>
<tr>
<th>Variable</th>
<th>Protocol-Directed Sedation (n = 162)</th>
<th>Non-Protocol-Directed Sedation (n = 159)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Continuous sedation infusion, No. (%)</td>
<td>66 (40.7)</td>
<td>66 (41.5)</td>
<td>.889</td>
</tr>
<tr>
<td>Continuous infusion agent, No. (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lorazepam</td>
<td>6 (9.1)</td>
<td>7 (10.6)</td>
<td>.770</td>
</tr>
<tr>
<td>Fentanyl</td>
<td>20 (30.3)</td>
<td>22 (33.3)</td>
<td>.709</td>
</tr>
<tr>
<td>Propofol</td>
<td>2 (3.0)</td>
<td>1 (1.5)</td>
<td>&gt;.999</td>
</tr>
<tr>
<td>Morphine</td>
<td>5 (7.6)</td>
<td>8 (12.1)</td>
<td>.381</td>
</tr>
<tr>
<td>Lorazepam and fentanyl</td>
<td>33 (50.0)</td>
<td>28 (42.4)</td>
<td>.383</td>
</tr>
<tr>
<td><strong>Duration of continuous infusion, days</strong></td>
<td><strong>3.5 ± 4.0</strong></td>
<td><strong>5.6 ± 6.4</strong></td>
<td><strong>.003</strong></td>
</tr>
<tr>
<td><strong>Duration of mechanical ventilation (hrs)</strong></td>
<td><strong>89.1 ± 133.6</strong></td>
<td><strong>124.0 ± 153.6</strong></td>
<td><strong>.003</strong></td>
</tr>
<tr>
<td><strong>Length of ICU stay (days)</strong></td>
<td><strong>5.7 ± 5.9</strong></td>
<td><strong>7.5 ± 6.5</strong></td>
<td><strong>.013</strong></td>
</tr>
<tr>
<td><strong>Length of hospital stay (days)</strong></td>
<td><strong>14.0 ± 17.3</strong></td>
<td><strong>19.9 ± 24.2</strong></td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Mortality, No. (%)</td>
<td>49 (30.3)</td>
<td>57 (35.9)</td>
<td>.342</td>
</tr>
<tr>
<td>Acquired organ system derangements</td>
<td>2.8 ± 1.4</td>
<td>2.9 ± 1.5</td>
<td>.737</td>
</tr>
<tr>
<td>Reintubation, No. (%)</td>
<td>14 (8.6)</td>
<td>21 (13.2)</td>
<td>.213</td>
</tr>
<tr>
<td>Tracheostomy, No. (%)</td>
<td>10 (6.2)</td>
<td>21 (13.2)</td>
<td>.038</td>
</tr>
</tbody>
</table>

ICU, intensive care unit.
Impact of Delirium and Coma on Mortality
Risk of Delirium with Benzodiazepines


\[\text{Risk of Delirium with Benzodiazepines}\]

**Figure:**
- **Graph 1:** Probability of transitioning to delirium vs. lorazepam dose (mg).
- **Graph 2:** Comparison of % days delirious between users and non-users for surgical and trauma patients.

**Notes:**
- Users vs. Non-Users: p=0.014 for Surgical, p=0.031 for Trauma.

*References:*
Engaging and Educating on the Importance of Monitoring for and Minimizing Delirium

Choosing a delirium screening tool
- TRIaled ICU-DSC and CAM-ICU

Formal education
- Nursing symposium
- Demonstrated how to use screening tool

Educational flyers

ICU-DSC: Intensive care unit delirium screening checklist
CAM-ICU: Confusion assessment method for the intensive care unit
Formal PAD Education Plan Across Multiple Disciplines

Multi-Disciplinary Educational Retreats in June 2013

- ABCDEF bundle
- Pros and cons of medications used to treat pain and agitation
- Harms of oversedation
- Importance of using validated scales to assess PAD
- Impact of sedation holidays/reductions on patient outcomes
- Rolled out our new intermittent dose protocol
- Importance of delirium monitoring
- Risks associated with delirium
- Demonstrated how to use the ICU-DSC
- Discussed our delirium guideline
- Pros and cons of antipsychotic therapy
Formal PAD Education Plan Across Multiple Disciplines

Nursing in-service/education
- Live and computer-based
- PAD guidelines
- Intermittent dose protocol
- Delirium monitoring

Provider in-service/education
- General PAD management
- Propofol infusion syndrome
- Ketamine

What changes are being made?
Why is it necessary?
How do we make the change?
What patients should receive the change?
SMH Adult Pain/Sedation Guideline for Mechanically Ventilated Patients

GENERAL PRINCIPLES......

• Intermittent bolus doses trialed before continuous infusions
• Hold continuous infusions on admission to the unit
• Optimize analgesia before initiating sedatives
• Promotes bolus doses
  • Anticipate and treat breakthrough pain/agitation
  • Prior to any increase in infusion rate
• Use of validated scales
  • Goal Non-verbal pain score 0-3 or numerical rating ≤ 5 on 0-10 scale
  • Goal SAS 3-4 unless specified different/paralyzed
• Reassess and document the level of sedation and analgesia every hour
SMH Adult Pain/Sedation Guideline for Mechanically Ventilated Patients

INTERMITTENT PAIN/SEDATION PROTOCOL......

**Hydromorphone** 1 mg IV every 5-15 min up to 3 doses for NVPS > 3  
- If NVPS≤3 start 1mg IV q2h prn  
- If NVPS> 3 after 3 doses initiate fentanyl infusion 50 mcg/hr

**Midazolam** 2 mg IV every 5-15 min up to 3 doses for SAS > 4  
- If SAS≤4 start 1mg IV q1h prn  
- If SAS>4 after 3 doses then initiate midazolam infusion at 2 mg/hr or if hemodynamically stable propofol infusion at 20 mcg/kg/min

*Provider can change doses based on individual patient needs*
Use of Computerized Provider Order Entry to Improve the Management of Pain/Agitation

Intermittent Pain and Sedation Protocol

Pain orderset

MAR instructions
**Use of Computerized Provider Order Entry to Improve the Management of Pain/Agitation**

<table>
<thead>
<tr>
<th>Medication</th>
<th>Dose</th>
<th>Route</th>
<th>Frequency</th>
<th>Additional Instructions</th>
</tr>
</thead>
<tbody>
<tr>
<td>midazolam (VERSED) injection 2 mg</td>
<td>2 mg</td>
<td>Intravenous</td>
<td>ONCE AS NEEDED for SAS &gt; 4</td>
<td>Administer per intermittent sedation management protocol: If SAS &gt; 4 give 2 mg IV x 1 and re-assess in 5-15 minutes, if SAS is still &gt; 4 then give another 2 mg IV x 1 and re-assess in 5 - 15 minutes, if SAS is still &gt; 4 then give a final dose of 2 mg IV x 1 and contact provider to order a midazolam or propofol infusion. A fentanyl infusion should be trialed prior to starting a midazolam or propofol infusion. If at any time the SAS is &lt;= 4 then stop subsequent x 1 orders and refer to the 1 mg IV q1h prn SAS &gt; 4 order for further sedation management. Ordered Admin Amount: 2 mL = 2 mg of 1 mg/mL</td>
</tr>
<tr>
<td>And midazolam (VERSED) injection 2 mg</td>
<td>2 mg</td>
<td>Intravenous</td>
<td>ONCE AS NEEDED for SAS &gt; 4</td>
<td></td>
</tr>
<tr>
<td>And midazolam (VERSED) injection 2 mg</td>
<td>2 mg</td>
<td>Intravenous</td>
<td>ONCE AS NEEDED for SAS &gt; 4</td>
<td></td>
</tr>
<tr>
<td>And midazolam (VERSED) injection 1 mg</td>
<td>1 mg</td>
<td>Intravenous</td>
<td>EVERY 1 HOUR PRN for SAS &gt; 4</td>
<td>If SAS&gt;4 on three consecutive assessments and analgesia has been optimized with a fentanyl infusion, consider switching prn order to a Midazolam or Propofol infusion</td>
</tr>
</tbody>
</table>

**Intermittent Pain and Sedation Protocol**

**Sedation orderset**

**MAR instructions**
Use of Computerized Provider Order Entry to Improve the Management of Pain and Agitation

Order Panel

MAR Administration Instructions

Midazolam Drip (Bolus + Continuous)

- midazolam (VERSED) 1 mg/ml bolus from infusion 0.5-10 mg
  0.5-10 mg EVERY 1 HOUR PRN, Intravenous, SAS score > 4, Starting Today at 1243, For 7 days

- midazolam (VERSED) 1 mg/ml IV Drip
  0.5-20 mg/hr CONTINUOUS (0.5-20 mL/hr), Intravenous, Starting Today at 1300, For 7 days

midazolam (VERSED) 1 mg/ml bolus from infusion 0.5-10 mg

Admin Instructions:
If sedation score > ordered goal, administer bolus dose equal to current rate.
Ordered Admin Amount: 0.5-10 mg

midazolam (VERSED) 1 mg/mL IV Drip

Admin Instructions:
Initiate midazolam infusion at 1 mg/hr.
Titrate to a SAS of 3-4.
If sedation score > ordered goal, administer bolus dose as ordered equal to current rate, and increase infusion by 1 mg/hr.
If SAS score at goal for 12 hours at same infusion rate, or if SAS score < goal, decrease infusion by 25%.
Notify provider if dose exceeds 4 mg/hr or if hemodynamically unstable.
Use of Computerized Provider Order Entry to Improve the Management of Pain and Agitation

NYS Regulation does not allow nurses to bolus propofol

URMC uses rapid titration strategy

Small doses of 10-20 mg are given every 5 minutes until SAS of 3-4 achieved then infusion rate is increased
Impact of an Analgesia-Based Sedation Protocol on Mechanically Ventilated Patients in a Medical Intensive Care Unit

- Retrospective Pre- and Post-Analgosedation guideline implementation study
- n=144
- Pre: Propofol infusion/prn narcotics → morphine infusion/midazolam
- Post: Fentanyl PRN or continuous/prn midazolam → propofol/dexmedetomidine

<table>
<thead>
<tr>
<th></th>
<th>Preintervention (2011 Group)</th>
<th>Postintervention (2013 Group)</th>
<th>95% CI</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Duration of mechanical ventilation (h), mean ± SD</td>
<td>138.3 ± 132.6</td>
<td>92.9 ± 73.3</td>
<td>-10.96 to -80.04</td>
<td>0.01</td>
</tr>
<tr>
<td>ICU length of stay (h), mean ± SD</td>
<td>211.5 ± 164.3</td>
<td>160.7 ± 125.7</td>
<td>-98.62 to -3.02</td>
<td>0.038</td>
</tr>
<tr>
<td>28-d ventilator-free days, mean ± SD</td>
<td>23.6 ± 4.9</td>
<td>24.1 ± 3.1</td>
<td>-0.8 to 1.8</td>
<td>0.47</td>
</tr>
<tr>
<td>28-d ventilator-free days (mortalities censored), mean ± SD</td>
<td>23.41 ± 5.51</td>
<td>24.57 ± 2.92</td>
<td>-0.51 to 2.84</td>
<td>0.17</td>
</tr>
<tr>
<td>RASS score, median (IQR)</td>
<td>-2.57 (-3.23 to -1.40)</td>
<td>-1.25 (-2.3 to -0.40)</td>
<td></td>
<td>0.001</td>
</tr>
<tr>
<td>% of RASS scores -3 to -5 in first 24 h, mean ± SD</td>
<td>46.8% ± 46.9%</td>
<td>27.3% ± 37.3%</td>
<td>-33.3 to -5.6</td>
<td>0.006</td>
</tr>
<tr>
<td>CPOT score, median (IQR)</td>
<td>2 (1.1–2.75)</td>
<td>1.5 (0.79–2.39)</td>
<td></td>
<td>0.03</td>
</tr>
<tr>
<td>Self-extubation, n (%)</td>
<td>2 (3.0)</td>
<td>5 (5.9)</td>
<td></td>
<td>0.46</td>
</tr>
<tr>
<td>Reintubation within 24 h of self-extubation, n (%)</td>
<td>1 (50)</td>
<td>2 (40)</td>
<td></td>
<td>1.00</td>
</tr>
<tr>
<td>Tracheostomy, n (%)</td>
<td>11 (16.9)</td>
<td>8 (10.1)</td>
<td></td>
<td>0.32</td>
</tr>
<tr>
<td>Hospital mortality, n (%)</td>
<td>22 (33.8)</td>
<td>24 (30)</td>
<td></td>
<td>0.72</td>
</tr>
</tbody>
</table>

Abbreviations: CI, confidence interval; COPD, chronic obstructive pulmonary disease; CPOT, Critical-Care Pain Observation Tool; ICU, intensive care unit; IQR, interquartile range; RASS, Richmond Agitation-Sedation Scale; SAPS, Simplified Acute Physiology score.

## Optimizing Non-Benzodiazepine Sedation

<table>
<thead>
<tr>
<th>Sedative</th>
<th>Indications</th>
<th>Monitoring</th>
</tr>
</thead>
</table>
| Propofol 10-80 mcg/kg/min | • Hemodynamically stable patients  
• Synergy with midazolam  
• Transition off of midazolam | • ↓ BP and HR  
• Propofol Infusion Syndrome  
-CK and TG 2-3x weekly  
-AGMA (lactate) |
| Dexmedetomidine 0.2-1.5 mcg/kg/hr | • Light sedation  
• Poor amnestic properties  
• Analgesic sparing  
• Facilitate extubation | • ↓ BP and HR  
• Tachyphylaxis |
| Ketamine 0.01-2 mg/kg/hr | • Hemodynamically unstable  
• Opioid tolerance  
• Bronchospasm  
• Analgesic effects | • ↑ BP and HR  
• Secretions  
• Delirium/psychosis |

BP=blood pressure; HR=heart rate; CK=creatine kinase; TG:Triglycerides; AGMA=anion gap metabolic acidosis
Pharmacist’s Role in Optimizing PAD Management

Enforce Guideline Recommendations on Rounds
- Decrease duration of mechanical ventilation
- Decrease ICU LOS
- Decrease Hospital LOS

Provide Nursing Education
- Oversedation reduced from 50% to 32%

Drive Sedation Management
- Decrease time on continuous sedation
- Reduce % patients on continuous sedation
- Decrease ICU and hospital LOS
- Reduce direct hospital costs and drug costs
Pharmacist’s Role in Optimizing PAD Management

Lead ABCDEF QI Initiatives
- Increase completion and pass rates with:
  - SAT safety screens
  - SAT on continuous infusions
  - Spontaneous breathing trial

Coordinate ABCDEF Bundle Collaboration
- Decrease ventilator days
- Decrease ICU LOS
- Reduce mortality

SAT: Sedation Awakening Trial

Pharmacist’s Role in Using Validated PAD Scales to Reduce Continuous Sedation

Is my patient on continuous infusions of sedatives and analgesics?

What have the SAS scores been over the last 12-24 hours?

If SAS <4 why......(vent dyssynchrony, extreme agitation, no reason)

• Can we decrease the rate?
• Has a sedation holiday been done?
• Can we change to intermittent sedation?
• Can we change to a non-benzodiazepine sedative?
Pharmacist’s Role in Using Validated PAD Scales to Reduce Continuous Sedation

- If SAS > 4 why......(pain, delirium, withdrawal)
  - Is the NVPS > 3?
    - Can we increase fentanyl, change to sedative with analgesic effects, what were they on at home?
  - Is the CAM-ICU positive?
    - Can we change to dexmedetomidine?
    - Should we add an antipsychotic?
    - Remove delirigenic meds/restraints/catheters
    - Non-pharmacologic therapy
    - Correct metabolic disturbances
- Are there any home medications we should restart?
- Have we tried coming down to quickly on the rates?
**TREATMENT ALGORITHM**

**Pain (NVPS > 3)**
- **Intermittent Analgesia**
  - Acetaminophen PO ATC or PRN mild/moderate pain
  - Hydromorphone IV PRN moderate/severe pain
  - Oxycodone PO PRN moderate/severe pain
- **Continuous Analgesedation**
  - Fentanyl infusion 25-250 mcg/hr
  - Ensure adequate bowel regimen
- **Sedative w/Analgesia**
  - Dexmedetomidine
  - Ketamine infusion

**Agitation (SAS > 4)**
- **CAM-ICU (-)**
  - **Intermittent Sedation**
    - Midazolam IV PRN
    - Haloperidol IV PRN
- **CAM-ICU (+)**
  - **Intermittent Sedation**
    - Haloperidol IV PRN
    - Quetiapine PO BID
  - **Continuous Sedation 1st Line:**
    - Dexmedetomidine (Light sedation)
  - **Continuous Sedation 2nd Line:**
    - **Propofol infusion**
      - Hemodynamically stable
    - **Midazolam infusion**
      - Hemodynamically unstable
    - **Refractory Agitation:**
      - Add on additional agent
      - Ketamine infusion
  - **Continuous Sedation 2nd Line:**
    - Fentanyl infusion (analgesedation)
    - Propofol infusion
    - Hemodynamically stable
Continuous Sedation Use Over Time on Our 12-Bed MICU

Number of Encounters Receiving Continuous Sedation

- 45-55% of all admitted patients are mechanically ventilated; 14% of mechanically ventilated patients receive continuous sedation
Snapshot of Current Sedation Practices in Our Adult ICUs

Select Month(s): 2017
All Adult ICUs

Total number of patients on a ventilator: n = 111

Average # of days on continuous sedation in last week: 2.23684
% of patients who have not started sedation: 30.28%
Total sedation days: 170

Intermittent sedation attempted prior to continuous?

Daily sedation interruption attempted in last 12 hrs?

Assessment for ventilator weaning attempted in last 12 hrs?

Medicine of the Highest Order
Snapshot of Current Sedation Practices in Our Adult ICUs

One Day Random Sample of ICU Patients

Percentage With One Assessment Completed in 24 hours

<table>
<thead>
<tr>
<th>Cohort 1</th>
<th>Cohort 2</th>
<th>Cohort 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>n=46</td>
<td>n=40</td>
<td>n=12</td>
</tr>
<tr>
<td>NVPS: 100%</td>
<td>NVPS: 100%</td>
<td>NVPS: 100%</td>
</tr>
<tr>
<td>SAS: 97.8%</td>
<td>SAS: 92.5%</td>
<td>SAS: 100%</td>
</tr>
<tr>
<td>CAM-ICU: 95.7%</td>
<td>CAM-ICU: 100%</td>
<td>CAM-ICU: 100%</td>
</tr>
<tr>
<td>Delirium present: 20.5%</td>
<td>Delirium present: 22.5%</td>
<td>Delirium present: 25%</td>
</tr>
</tbody>
</table>
Continuous Improvement is Better Than Delayed Perfection

Mark Twain

NEXT STEPS.....

Pharmacist coordination of ABCDEF Bundle
  • Use of clinical decision support in the electronic medical record

Standardizing provider note template
  • Treat PAD scores as “vital signs”

Revitalize delirium awareness, monitoring, and management
  • Fall of 2017 retreats