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Sedation Pearls & Pitfalls

March 2, 2022

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Advanced Clinical Pharmacist, Critical Care
Intermountain Medical Center
Objectives

1. Understand how to improve patient outcomes using analgosedation principles for sedation management

2. Apply existing evidence in order to thoughtfully consider a bolus vs. continuous sedation approach

3. Review sedation options and pearls for nonintubated patients

No disclosures
Analgosedation
## Sedation: Long Term Impact, Mortality

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Incidence</th>
<th>Risk Factors</th>
</tr>
</thead>
</table>
| Cognitive impairment          | 30-80%     | Delirium, presence and duration  
Sedation  
Hypo and hyperglycemia  
Hypoxemia, Hypotension       |
| Psychiatric illness, PTSD     | Up to 57%  | Sedation  
Poor recall of intensive care unit (ICU) stay  
Younger age                 |
| Physical impairment           | 25-80%     | Acute Respiratory Distress Syndrome (ARDS)  
Prolonged mechanical ventilator (MV) time  
Sepsis, Multi-organ failure  
Steroid use                  |

Devlin JW et al. Crit Care Med 2018; 46e825-873
Treatment Guidance

**PADIS**
- Pain
- Agitation/Sedation
- Delirium
- Immobility
- Sleep Disruption

**ABCDEF Bundle**
- Assess and manage pain
- Breathing trials, spontaneous awakening
- Choice of sedative
- Daily delirium monitoring
- Early mobility
- Family engagement and empowerment

Devlin JW et al. Crit Care Med 2018; 46e825-873
Key Principles

Non-modifiable Risk: Delirium
- Older age
- Dementia
- Emergency surgery or trauma
- High APACHE

Analgesedation
- Treat pain first
- Exceptions exist

Establish Goals
- Patient-specific
- Least-effective doses

Non-medication
- Music, pet therapy
- Cold packs
- Cognition exercises
- Reorientation
- Early mobility
- Hearing/vision
- Sleep/wake cycle

Validated Scales
- Behavioral Pain Scale (BPS)
- Critical care pain observation tool (CPOT)
- Richmond Agitation-Sedation Scale (RASS)

# Behavioral Pain Scale (BPS)

<table>
<thead>
<tr>
<th>Item</th>
<th>Description</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Facial Expression</strong></td>
<td>Relaxed</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Partially tightened (e.g. brow lowering)</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>Fully tightened (e.g. eyelid closing)</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>Grimacing</td>
<td>4</td>
</tr>
<tr>
<td><strong>Upper Limbs</strong></td>
<td>No movement</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Partially bent</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>Fully bent with finger flexion</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>Permanently retracted</td>
<td>4</td>
</tr>
<tr>
<td><strong>Compliance with Ventilation</strong></td>
<td>Tolerating movement</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Coughing with movement</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>Fighting ventilator</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>Unable to control ventilation</td>
<td>4</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Indicator</th>
<th>Description</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Facial Expression</strong></td>
<td>No muscular tension observed</td>
<td>Relaxed, neutral</td>
</tr>
<tr>
<td></td>
<td>Presence of frowning, brow lowering, orbit tightening</td>
<td>Tense</td>
</tr>
<tr>
<td></td>
<td>All of the above plus eyelids tightly closed</td>
<td>Grimacing</td>
</tr>
<tr>
<td><strong>Body Movement</strong></td>
<td>Does not move at all</td>
<td>Absence of movement</td>
</tr>
<tr>
<td></td>
<td>Slow cautious movements, touching site, seeks attention through movement</td>
<td>Protection</td>
</tr>
<tr>
<td></td>
<td>Pulling tube, attempting to sit up or climb out of bed, moving limbs/thrashing/striking out, not following commands</td>
<td>Restlessness</td>
</tr>
<tr>
<td><strong>Muscle tension</strong></td>
<td>No resistance to passive movements</td>
<td>Relaxed</td>
</tr>
<tr>
<td></td>
<td>Resistance to passive movements</td>
<td>Tense, rigid</td>
</tr>
<tr>
<td></td>
<td>Strong resistance to passive movements, inability to complete them</td>
<td>Very tense or rigid</td>
</tr>
<tr>
<td><strong>Compliance with ventilator (intubated)</strong></td>
<td>Alarms not activated, easy ventilation</td>
<td>Tolerating vent or movement</td>
</tr>
<tr>
<td></td>
<td>Alarms stop spontaneously</td>
<td>Coughing but tolerating</td>
</tr>
<tr>
<td></td>
<td>Asynchrony: blocking ventilation, alarms frequently activated</td>
<td>Fighting ventilator</td>
</tr>
<tr>
<td><strong>Vocalization (extubated)</strong></td>
<td>Talking in normal tone or no sound</td>
<td>Talking normal or no sound</td>
</tr>
<tr>
<td></td>
<td>Sighing, moaning</td>
<td>Sighing, moaning</td>
</tr>
<tr>
<td></td>
<td>Crying out, sobbing</td>
<td>Crying out, sobbing</td>
</tr>
</tbody>
</table>

Multimodal Approach

Non-Opioid:
• Acetaminophen
• Gabapentin, Pregabalin
• Carbamazepine
• Lidocaine patches
• Ketamine

Non-Medication:
• Ice packs/Heat
• Cognitive distraction
• Music/Pet therapy
• Massage
• Setting Expectations

Non-Opioid

Non-Medication

Opioid
# Opioids & Ketamine

<table>
<thead>
<tr>
<th>Drug</th>
<th>Onset</th>
<th>Duration</th>
<th>Bolus Dosing</th>
<th>IV Infusion Rates</th>
<th>Pearls</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fentanyl</td>
<td>10-30 sec</td>
<td>30-60 min</td>
<td>25-100 mcg q1h PRN</td>
<td>10-200 mcg/h</td>
<td>Less hypotension than morphine</td>
</tr>
<tr>
<td>Hydromorphone</td>
<td>5 min</td>
<td>3-4 h</td>
<td>0.5-1 mg q1h PRN</td>
<td>0.2-3 mg/h</td>
<td>Option if tachyphylaxis to fentanyl</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Increased drug exposure in renal impairment</td>
</tr>
<tr>
<td>Morphine</td>
<td>5-10 min</td>
<td>3-5 h</td>
<td>2–8 mg q2h PRN</td>
<td>1-10 mg/h</td>
<td>Histamine release</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Active metabolites</td>
</tr>
<tr>
<td>Ketamine</td>
<td>30-40 sec</td>
<td>15-20 min</td>
<td>0.25-1 mg/kg q2h PRN</td>
<td>1-10 mg/h</td>
<td>Adjunct pain dosing</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Attenuates opioid tolerance</td>
</tr>
</tbody>
</table>
## Non-Opioids

<table>
<thead>
<tr>
<th>Drug</th>
<th>Onset</th>
<th>Duration</th>
<th>Dosing</th>
<th>Pearls</th>
</tr>
</thead>
<tbody>
<tr>
<td>APAP (PO,PR)</td>
<td>30-60 min</td>
<td>4-6 h</td>
<td>325-1000 mg Q4-6h (MDD 4g/d)</td>
<td>Hepatic dysfunction max 3g/d or avoid</td>
</tr>
<tr>
<td>APAP (IV)</td>
<td>5-10 min</td>
<td>4-6 h</td>
<td>1000 mg IV Q6H (MDD 4g/d)</td>
<td></td>
</tr>
<tr>
<td>Ketorolac (IM/IV)</td>
<td>10-20 min</td>
<td>4-6 h</td>
<td>15-30 mg IM/IV Q6H up to 5 days (MD = 120 mg/d x 5d)</td>
<td>Avoid NSAIDs in most ICU patients Increased drug exposure in geriatric</td>
</tr>
<tr>
<td>Ibuprofen</td>
<td>25 min</td>
<td>4-6 h</td>
<td>400 mg PO Q4H (MDD 2.4 g/d)</td>
<td></td>
</tr>
<tr>
<td>Gabapentin</td>
<td>1-4 h</td>
<td>5-7h</td>
<td>100 mg PO TID; (MDD 900-3600 mg/d)</td>
<td>Sedation, confusion, dizziness, ataxia Adjust in renal failure May have impaired absorption</td>
</tr>
</tbody>
</table>
Bolus vs Continuous Infusion

Pain & Sedation
Sedation

Goals
- Reduce anxiety and stress
- Prevent harm
- Ventilator compliance

Morbidity
- ICU length of stay (LOS)
- Duration of MV
- Physical function
- Neurocognitive and psychologic outcomes

ICU Pitfalls
- Validated scales
- Unpredictable pharmacokinetics
- Drug interactions
- Organ dysfunction
- Absorption variability
- Hemodynamic instability

Devlin JW et al. Crit Care Med 2018; 46e825-873
Light Sedation

How to apply in practice with the available evidence
Purpose: Is minimal sedation feasible and without major adverse events?

<table>
<thead>
<tr>
<th>Design</th>
<th>Prospective, observational 2-month period</th>
</tr>
</thead>
<tbody>
<tr>
<td>Population</td>
<td>ICU patients &gt; 12 hours</td>
</tr>
<tr>
<td>Descriptive outcomes</td>
<td>• Admit diagnosis</td>
</tr>
<tr>
<td></td>
<td>• Severity of illness</td>
</tr>
<tr>
<td></td>
<td>• Sedatives/opiates</td>
</tr>
<tr>
<td></td>
<td>• Self-extubation</td>
</tr>
<tr>
<td></td>
<td>• Duration of MV</td>
</tr>
<tr>
<td></td>
<td>• ICU LOS</td>
</tr>
<tr>
<td></td>
<td>• 28-day mortality</td>
</tr>
</tbody>
</table>
Salgado DR, et al

- Total = 335 patients; MV = 145 (46%)
- Sedation received = 142 (42%)
  - 85% MV
  - Intermittent bolus = 20 (14%)
  - Continuous infusion = 122 (86%)
    - MV (92% vs 18%) and ARDS (19% vs 0%)
    - Longer median ICU LOS [24 (12-36) vs 16 (8-24) p < 0.01]
    - Greater risk of death [HR 2.82 (0.66-12) p 0.16]
- Self-extubation = 6; 1 reintubated
- 14 patients received haloperidol

Salgado DR et al. Journal of Critical Care (2011) 26, 113-121
<table>
<thead>
<tr>
<th></th>
<th>No mechanical ventilation (n = 180)</th>
<th>Mechanical ventilation (n = 155)</th>
<th>( P )</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Sedation</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Strategy of sedation, n (%)</td>
<td>Continuous 2 (1)</td>
<td>120 (77)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td></td>
<td>Intermittent 9 (5)</td>
<td>11 (7)</td>
<td></td>
</tr>
<tr>
<td>Type of sedative drug, n (%)</td>
<td>Midazolam 6 (3)</td>
<td>70 (45)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td></td>
<td>Propofol 1 (1)</td>
<td>68 (44)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Diazepam 9 (5)</td>
<td>7 (5)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Thiopental 0</td>
<td>2 (1)</td>
<td></td>
</tr>
<tr>
<td>Duration of sedation (h)</td>
<td>0 (0-0)</td>
<td>5 (1-18)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Sedative max dose</td>
<td>Midazolam (mg/h) 2.5 (2-3)</td>
<td>5 (2.5-10)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td></td>
<td>Propofol (mg/h) 20</td>
<td>200 (100-240)</td>
<td>NA</td>
</tr>
<tr>
<td>Sedative total dose</td>
<td>Midazolam (mg) 3.5 (3-4)</td>
<td>74.5 (18-178)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td></td>
<td>Propofol (mg) 40</td>
<td>470 (240-1170)</td>
<td>NA</td>
</tr>
<tr>
<td><strong>Analgesia</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Strategy of analgesia, n (%)</td>
<td>Continuous 15 (8)</td>
<td>108 (70)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td></td>
<td>Intermittent 71 (39)</td>
<td>25 (16)</td>
<td></td>
</tr>
<tr>
<td>Type of analgesic drug, n (%)</td>
<td>Morphine 65 (36)</td>
<td>115 (74)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td></td>
<td>Remifentanil 0</td>
<td>42 (27)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Fentanyl 0</td>
<td>1 (1)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Paracetamol 88 (49)</td>
<td>60 (39)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Others a 8 (4)</td>
<td>7 (11)</td>
<td></td>
</tr>
<tr>
<td>Duration of analgesia (h)</td>
<td>0 (0-2)</td>
<td>19 (3.41)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Analgesia max dose</td>
<td>Morphine (mg/h) 2 (2-2)</td>
<td>2 (2-4)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td></td>
<td>Remifentanil (mg/h) 0</td>
<td>0.5 (0.2-1.1)</td>
<td>NA</td>
</tr>
<tr>
<td>Analgesia total dose</td>
<td>Morphine (mg) 8 (3.5-17)</td>
<td>67 (25.5-162)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td></td>
<td>Remifentanil (mg) 0</td>
<td>24 (22.1-99.1)</td>
<td>NA</td>
</tr>
<tr>
<td>Coinfusion of sedation and opiates, n (%)</td>
<td>0 (0)</td>
<td>96 (62)</td>
<td>&lt;.001</td>
</tr>
</tbody>
</table>

Data are presented as n (%) or median (25%-75% interquartile range). NA indicates not applicable; max: maximum.

* Nonsteroidal anti-inflammatory drugs, tramadol.
Salgado DR, et al

MV without continuous sedation was safely achieved more than 80% of the time

- Continuous infusion and intermittent bolus approaches used
- No direct comparison of intermittent vs continuous strategy

No major adverse effects

- Not well evaluated

No difference in ICU LOS or time on MV

Other long-term sequelae not evaluated
**Strom T, et al**

**Purpose:** Is duration of MV reduced when using a no sedation vs daily sedation interruption protocol?

<table>
<thead>
<tr>
<th>Design</th>
<th>Prospective, randomized controlled trial</th>
</tr>
</thead>
<tbody>
<tr>
<td>Population</td>
<td>ICU patients requiring MV for &gt; 24h</td>
</tr>
<tr>
<td>Intervention</td>
<td></td>
</tr>
<tr>
<td><strong>No Sedation (n = 55)</strong></td>
<td>• Morphine 2.5-5 mg bolus prn</td>
</tr>
<tr>
<td></td>
<td>• Propofol x48h → midazolam infusion; daily interruption</td>
</tr>
<tr>
<td></td>
<td>• Morphine 2.5-5 mg bolus prn</td>
</tr>
<tr>
<td><strong>Sedation (n = 58)</strong></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Days without MV (28d period)</td>
</tr>
<tr>
<td></td>
<td>• ICU and hospital LOS</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>No sedation (n=55)</th>
<th>Sedation (n=58)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Days without mechanical ventilation (from intubation to day 28)</td>
<td>13·8 (11·0; 18·0)</td>
<td>9·6 (10·0; 6·9)</td>
<td>0·0191*†</td>
</tr>
<tr>
<td>Length of stay (days)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intensive care unit</td>
<td>13·1 (5·7; 23·3)†</td>
<td>22·8 (11·7; 34·0)</td>
<td>0·0316*§</td>
</tr>
<tr>
<td>Hospital</td>
<td>34 (17·65)</td>
<td>58 (33·85)</td>
<td>0·0039*¶</td>
</tr>
<tr>
<td>Mortality</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intensive care unit</td>
<td>12 (22%)</td>
<td>22 (38%)</td>
<td>0·06</td>
</tr>
<tr>
<td>Hospital</td>
<td>20 (36%)</td>
<td>27 (47%)</td>
<td>0·27</td>
</tr>
<tr>
<td>Drug doses (mg/kg)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Propofol (per h of infusion)**</td>
<td>0 (0·0·515)</td>
<td>0·773 (0·154; 1·648)</td>
<td>0·0001</td>
</tr>
<tr>
<td>Midazolam (per h of infusion)</td>
<td>0 (0·0)</td>
<td>0·0034 (0·0·0240)</td>
<td>&lt;0·0001</td>
</tr>
<tr>
<td>Morphine (per h of mechanical ventilation)</td>
<td>0·0048 (0·0·014; 0·0111)</td>
<td>0·0045 (0·0·020; 0·0064)</td>
<td>0·39</td>
</tr>
<tr>
<td>Haloperidol (per day of mechanical ventilation)</td>
<td>0 (0·0)</td>
<td>0 (0·0)</td>
<td>0·0140</td>
</tr>
<tr>
<td>Tracheostomy</td>
<td>16 (29%)</td>
<td>17 (29%)</td>
<td>0·98</td>
</tr>
<tr>
<td>Ventilator-associated pneumonia</td>
<td>6 (11%)</td>
<td>7 (12%)</td>
<td>0·85</td>
</tr>
</tbody>
</table>

Data are mean (SD), median (IQR), or number (%). †data not available because of censoring at day 28. *Corrected for baseline variables: age, sex, weight, acute physiology and chronic health evaluation (APACHE II), simplified acute physiology score (SAPS II), and sequential organ-failure assessment (SOFA) at day 1. †Calculated from multiple linear regression. ‡More than 25% of patients remained in the intensive care unit for more than 28 days (figure 2). §Calculated from Cox regression analysis. ¶Calculated for the first 30 days to agree with the proportional hazards assumption. ||Drug dose (mg) as a proportion of bodyweight (kg). **Maximum dose during 48 h of treatment.

Table 2: Outcome data
Strom T, et al

Providing analgesia with intermittent boluses may be an effective strategy to maintain ventilator compliance, while reducing duration of MV and ICU LOS

Pitfalls:

- Change from propofol to midazolam infusion
- Morphine not commonly used
- Delirium detection was not a primary outcome
- Did not evaluate other patient centered outcomes
Continuous Infusion

Specific patient populations
- Severe ARDS
- Ventilator compliance
- Withdrawal syndromes
- Intracranial hypertension or seizure management
- Neuromuscular blockade

Non-benzodiazepine preferred
- Shorter ICU LOS
- Shorter duration of MV
- Reduced incidence of delirium

Daily sedation vacations

Devlin JW et al. Crit Care Med 2018; 46e825-873
Continuous Infusion

Evidence Pitfalls

• Benzodiazepine-heavy approach
  o Finfer, et al: intermittent diazepam vs continuous midazolam
    ▪ No difference: hours to or within target sedation, over sedation
  o Carson, et al: intermittent lorazepam vs continuous propofol
    ▪ Propofol group: fewer days on ventilator, reduced ICU LOS

• Evidence supporting sedation vacation is in the setting of continuous infusion

• “Light sedation” not well-defined
  o RASS -2 to +1
  o Need more robust correlation with clinical outcomes

**Intermittent Bolus**

May be a reasonable approach for some patients

- Wean continuous infusions
- Avoid dose escalations
- In place of continuous infusions
  - Minimal ventilator settings
  - Anticipated short duration of MV
  - Altered mental status due to unknown cause
  - Hemodynamic compromise

**Drug Shortages**

- Often require lower cumulative doses

---

Vinayak AG *CHEST Counterpoint* 2012, 142:5.
# Traditional Sedatives

<table>
<thead>
<tr>
<th>Drug</th>
<th>Bolus Dosing</th>
<th>IV Infusion</th>
<th>Pearls</th>
</tr>
</thead>
<tbody>
<tr>
<td>Midazolam</td>
<td>2-5 mg q1-2h PRN</td>
<td>0.5-10 mg/h</td>
<td>One active metabolite</td>
</tr>
<tr>
<td>Lorazepam</td>
<td>2-4 mg q1-2h PRN</td>
<td>Avoid</td>
<td>Propylene glycol toxicity</td>
</tr>
<tr>
<td>Diazepam</td>
<td>5-10 mg q2-4h PRN</td>
<td>Avoid</td>
<td>Vesicant: can cause phlebitis. Longer acting: two active metabolites</td>
</tr>
<tr>
<td>Propofol</td>
<td>0.5-2 mg/kg Procedural or to avoid dose escalation</td>
<td>5-75 mcg/kg/min</td>
<td>+/- Hypotension Hypertriglyceridemia Propofol Related Infusion Syndrome (PRIS)</td>
</tr>
<tr>
<td>Dexmedetomidine</td>
<td>Avoid</td>
<td>0.1-1.5 mcg/kg/h</td>
<td>Bradycardia. Start low, go slow Does not cause amnesia or deep sedation</td>
</tr>
<tr>
<td>Ketamine</td>
<td>0.5-2 mg/kg Procedural or to avoid dose escalation Stand-alone</td>
<td>5-75 mcg/kg/min</td>
<td>Continuous sedation dosing. Emergence reactions. Hallucinations/Agitation. Catecholamine depletion → myocardial depression</td>
</tr>
</tbody>
</table>

Lexicomp Onlinee, Lexi-Drugs, Hudson, Ohio: Lexi-Comp, Inc; April 29, 2018
Non-traditional Sedatives

Phenobarbital (MDD = 400 mg)
- PRN Bolus: 2-5 mg/kg IV q4h PRN vs. 130-260 mg IV q4h PRN
- Load: 5-10 mg/kg IV x1
- Pearls:
  - Slow IV push, max 60 mg/min. Large doses in IVPB
  - Many drug interactions
  - +/- bradycardia, hypotension

Valproic Acid
- 500 mg IV or enteral BID to TID, +/- 30 mg/kg loading dose
- Pearls:
  - +/- thrombocytopenia, transaminitis, hyperammonemia
  - Drug interaction with carbapenems

Clonidine: alpha-2 agonist
- 0.2-0.3 mg q6-8h scheduled, up to 0.4 mg q6h
- If tapering off dexmedetomidine, reduce infusion by 25% with each dose

Agitation Management in the Nonintubated Patient
Agitation in the ICU

- Pain
- Delirium
- Sleep-wake disturbances
- Fear, anxiety
- Encephalopathy
- Infection/Fever
- Brain injury/Trauma
- Medications
- Metabolic disorders
- External stimuli
- Underlying psychiatric disorders
- Substance abuse or withdrawal
- Toxins

Medication Options for Nonintubated Patients

• Antipsychotics
• Benzodiazepines
• Ketamine (low dose)
• Dexmedetomidine (low dose)
• Clonidine
• Valproic Acid
• Phenobarbital
• Opioids
• Non-opioid analgesics
• Sleep promoting medications
Delirium

Strong Modifiable Risk Factors
- Benzodiazepine use
- Blood transfusions

Moderate Modifiable Risk Factors
- Use of psychoactive medication
- Hypertension
- Neurologic disease on admission
- Trauma
- Dialysis or CVVHD
- History of respiratory disease

Confusion Assessment Method - ICU

[Flowchart image showing the assessment process]

Devlin JW et al. Crit Care Med 2018; 46e825-873
Delirium Prevention & Treatment

Multimodal non-medication interventions, ABCDEF bundle

• Reduce modifiable risk factors
• Improve cognition
• Optimize sleep, improve daytime wakefulness
• Increase early mobilization, physical rehabilitation
• Hearing and vision
• Re-direct, de-escalate

Significant distress: anxiety, fear, hallucinations, self harm, harm to others

• Short term use of atypical antipsychotics or haloperidol

Violent/aggressive agitation or prohibiting cares

• IM sedatives or antipsychotics
• Dexmedetomidine
• Physical restraints

Devlin JW et al. Crit Care Med 2018; 46e825-873
Antipsychotics

First line use
- Psychosis

Possible use
- Undifferentiated agitation
- Agitated Delirium
- Intoxication-related agitation

First Generation (FGA)
- Haloperidol
- Droperidol

Second Generation (SGA): less sedating, fewer extrapyramidal side effects
- Olanzapine
- Quetiapine
- Risperidone
- Ziprasidone

# SGA

<table>
<thead>
<tr>
<th>Drug</th>
<th>Onset</th>
<th>Duration</th>
<th>Dosing</th>
<th>Pearls</th>
</tr>
</thead>
<tbody>
<tr>
<td>Olanzapine</td>
<td>ODT: &lt;60 min</td>
<td>ODT: n/a</td>
<td>ODT: 5-10 mg TID (MDD 30 mg/d) IM: 5-10 mg x1, repeat at 2 hr then 4 hr IV: 5 mg x1, repeat 2.5-5 mg in 10 min (MDD 10 mg/d)</td>
<td>Avoid IV use due to risk of respiratory depression Least QTc prolonging Faster oral onset compared to oral risperidone</td>
</tr>
<tr>
<td></td>
<td>IM: 15 min</td>
<td>IM: 2 hr</td>
<td>IM: 5-10 mg x1, repeat at 2 hr then 4 hr</td>
<td></td>
</tr>
<tr>
<td></td>
<td>IV: 5-10 min</td>
<td>IV: n/a</td>
<td>IV: n/a</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Risperidone</td>
<td>60 min</td>
<td>Variable</td>
<td>ODT: 1-2 mg q2-6 hr (MDD 6 mg/d)</td>
<td>Higher doses in schizophrenia</td>
</tr>
<tr>
<td>Ziprasidone</td>
<td>IM: 15-30 min</td>
<td>IM: 2-8 hr</td>
<td>IM: 10-20 mg x1, repeat at 2-4 hr (MDD 40 mg/d) PO: 20-40 mg BID (MDD 80 mg)</td>
<td>Highest QTc prolongation of SGA</td>
</tr>
<tr>
<td></td>
<td>PO: n/a</td>
<td>PO: 8-12 hr</td>
<td></td>
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<td></td>
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<td></td>
</tr>
<tr>
<td>Quetiapine</td>
<td>30-90 min</td>
<td>6-12 hr</td>
<td>12.5-400 mg/d, can be divided BID or TID (MDD 400 mg/d for agitation)</td>
<td>Higher doses in schizophrenia</td>
</tr>
<tr>
<td>Drug</td>
<td>Onset</td>
<td>Duration</td>
<td>Dosing</td>
<td>Pearls</td>
</tr>
<tr>
<td>------------</td>
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<td>---------------------------------------------</td>
<td>------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Haloperidol</td>
<td>IM: 15 min</td>
<td>IM: 2 hr</td>
<td>IM or IV: 2-10 mg every 15 min – 6 hr</td>
<td>Lactate formulation may be given IV or IM</td>
</tr>
<tr>
<td></td>
<td>IV: 3-15 min</td>
<td>IV: 3-24 hr</td>
<td>(MDD 30 mg/d)</td>
<td>Decanoate formulation can only be given IM</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>PO rarely used</td>
</tr>
<tr>
<td>Droperidol</td>
<td>IM/IV: 2-10 min</td>
<td>2-4 hr</td>
<td>IM or IV: 2.5-10 mg x1 (MDD 10-20 mg/d)</td>
<td>Decreased combativeness significantly more than haloperidol when given IM</td>
</tr>
</tbody>
</table>
Sleep Disruption in the ICU

Often normal in ICU patients:
• Total sleep time
• Sleep efficiency

Often greater in ICU patients:
• Sleep fragmentation
• Light sleep (stages 1 & 2)
• Daytime Sleep (up to 57%)

Often decreased in ICU patients:
• Deep sleep (REM, slow wave)
• Sleep quality

Devlin JW et al. Crit Care Med 2018; 46e825-873
Sleep Improvement

Prioritize non-medication strategies

• Noise and light reduction
• Daytime activity
• Earplugs, eyeshades

Medications only after careful consideration

- Melatonin 3-10 mg qHS +/-
- Ramelteon 8 mg qHS +/-
- Antipsychotics
  - Tricyclic antidepressants +/-
  - Benzodiazepines
- Trazodone 12.5–200 mg qHS +/-
- Dexmedetomidine +/-

Devlin JW et al. Crit Care Med 2018; 46e825-873
Matthews EE, AACN Adv Crit Care. 2011; 22(3):204-224
Dexmedetomidine and Sleep

Sleep architecture
- Endogenous sleep-promoting pathway
- Animal and preclinical settings

Sleep in MV patients
- Alexopoulou C et al: 13 patients on MV, no other sedation
  - Significantly higher sleep efficiency, reduced stage 1 and 2 sleep, increased proportion of night time sleep

Sleep in non-MV patients
- Wu XH et al: RCT of 76 patients age ≥65 admitted to ICU after noncardiac surgery without MV
  - Significantly increased % stage N2 sleep (15.8% vs 43.5%), but no difference on N3 or REM sleep
  - Longer total sleep time, increased sleep efficiency, improved subjective sleep quality
  - Increased incidence of hypotension in dexmedetomidine group

Wu XH et al. Anesthesiology 2016, 125, 979-991.
Today’s Accomplishments

1. Understand how to improve patient outcomes using analgosedation principles for sedation management

2. Apply existing evidence in order to thoughtfully consider a bolus vs. continuous sedation approach

3. Review sedation options and pearls for nonintubated patients
Discussion & Questions