ICU Best Practices, Sedation, Pressors

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Objectives

- Understand the use of an ICU best practices bundle in the daily progress note to improve outcomes of critically ill patients
- Understand indications for, selection of, and management of pharmacologic sedation in critically ill patients
- Understand indications for, selection of, and management of vasopressor agents in critically ill patients
ICU Best Practices/Prevention

ABC DEF, FAST HUG BID, OH MY...
Best Practice/Prevention Bundles

F
Feeding

A
Analgesia

S
Sedation

T
Thromboembolic prophylaxis

H
Head of bed elevation

U
Ulcer (stress) prophylaxis

G
Glycemic control

S
Spontaneous breathing trial

B
Bowel regimen

I
Indwelling catheter removal

D
De-escalation of antibiotics

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Table. ABCDEF Bundle

<p>| | |</p>
<table>
<thead>
<tr>
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</thead>
<tbody>
<tr>
<td>A</td>
<td>Assess, prevent, and manage pain</td>
</tr>
<tr>
<td>B</td>
<td>Both spontaneous awakening &amp; breathing trials</td>
</tr>
<tr>
<td>C</td>
<td>Choice of medication management</td>
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<tr>
<td>D</td>
<td>Delirium</td>
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<tr>
<td>E</td>
<td>Early mobility &amp; exercise</td>
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<tr>
<td>F</td>
<td>Family engagement and empowerment</td>
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Hard Data on ABCDEF

- Prospective cohort study of 15k adults in ICU
  - Less death (HR 0.32 (0.17-0.62))
  - Less mechanical ventilation (OR 0.28 (0.22-0.36))
  - Less coma (OR 0.35 (0.22-0.56))
  - Also less delirium, restraint use, ICU readmission
  - Dose-response relationship between number of components used and effects

- Another study: reduced self-perceived patient discomfort
  - Followup study: less PTSD at 1 year
**Critical Care Best Practices**

- Assess/prevent/manage pain:
- Both spontaneous awakening and breathing trials?
- Choice of analgesia & sedation:
- Delirium assessment/prevention/management:
- Early mobility?
- Family involvement/updates:

**Nutrition plan:**
Thromboprophylaxis:
VAP prophylaxis:
Gastric acid suppression (if intubated or home Rx):
Glycemic control:
Bowel regimen ordered (last BM: ***):
Line/device assessment:
Antibiotic de-escalation:

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**Analysis:**

- Analgesia: 35486
- SAT and SBT: 35487
- Choice of Sedation: 35488

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**Critical Care Best Practices**

- Assess/prevent/manage pain: Yes.
- Both spontaneous awakening and breathing trials?: No
- Choice of analgesia & sedation: Reviewed. Continue current plan
- Delirium assessment/prevention/management: Assessment/prevention ongoing
- Early mobility?: No.
- Family involvement/updates: Yes

**Nutrition plan:**
- Tube feeds
- Chemical
- Mechanical
- HOB > 30 degrees and chlorhexidine
- H2 antagonist
- Insulin infusion
- Yes
- Reviewed & no changes

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**Notes:**

- **ICU Best Practices**
- **ICU HPC Consult**
- **ANW Intensivists Notes**
Sedation

Milk of Amnesia and other treats...
Sedation – Why?

- Distress usually presents as a agitation
- Reduce distress
  - Patient comfort
  - Reduces sympathetic tone
  - Agitation interferes with care (e.g. ventilator asynchrony)
Sedation – When?

- For observed, not anticipated distress
  - Otherwise likely oversedation, which leads to worse clinical outcomes
  - Sedation for procedures is an exception

- When you can’t fix the distress by
  - Treating an underlying cause directly:
    - Anxiety, Pain, Dyspnea, Delirium
  - Using nonpharmacologic interventions:
    - Reassurance, family support, sleep hygiene, music, relaxation
Not Sedation:

- **Physical restraints:**
  - An adjunct to sedation for managing distress, not a sole/primary intervention
  - Remove restraints as soon as possible

- **Neuromuscular blockade:**
  - Not sedation or analgesia or anxiolytic
  - Call your friendly neighborhood intensivist
Sedation – Choice of Agent

- No superior agent/class for all situations
  - General rule: treat pain with narcotics first

- Options:
  - Benzodiazepines
  - Opioids
  - Propofol
  - Dexmedetomidine (Precedex)
  - Ketamine
  - Antipsychotics (not sedation)
Based on cause of distress

- Dyspnea: opioids
- Pain: opioids
- Delirium: dexmedetomidine, antipsychotics
- Anxiety: propofol, dexmedetomidine, benzodiazepines*
- Multifactorial: consider combination therapy. Treat pain first.

*Society of Critical Care Medicine: avoid benzodiazepines because shorter duration of mechanical ventilation demonstrated with other agents. Recommend propofol for cardiac patients; propofol or dexmedetomidine for other patients.
<table>
<thead>
<tr>
<th>Agent</th>
<th>Advantages</th>
<th>Disadvantages</th>
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<tbody>
<tr>
<td>Fentanyl (not an amnestic)</td>
<td><strong>Strong analgesia</strong>, strong sedation, immediate onset, less hypotension</td>
<td>Lipophilic accumulation</td>
</tr>
<tr>
<td>Propofol (not an analgesic)</td>
<td>Strong sedation, immediate onset, rapid awakening (when used short-term), no hepatic or renal adjustments, little interaction, easy to titrate, antiepileptic</td>
<td>Hypotension, bradycardia, respiratory depression, lipophilic accumulation (debated)</td>
</tr>
<tr>
<td>Ketamine (not an amnestic)</td>
<td>Dissociative analgesic, maintains blood pressure, +/- reduced opioid tolerance</td>
<td>Off label use, increased sympathetic tone, hallucinations, delirium</td>
</tr>
<tr>
<td>Dexmedetomidine (central alpha-2 agonist)</td>
<td>Sedative sympatholytic, moderate anxiolysis and analgesia, may cause less delirium, may reduce vent days</td>
<td>Hypotension, hypertension, bradycardia (may persist after drug stopped)</td>
</tr>
<tr>
<td>Midazolam</td>
<td>Strong amnestic and anxiolytic, immediate onset, short duration (when used short-term)</td>
<td>Active metabolites accumulate in long-term use, lipophilic accumulation delirium, interactions</td>
</tr>
<tr>
<td>Haloperidol</td>
<td>Moderately sedating, minimal effect on vitals, IV formulation</td>
<td>Increasing half-life with additional doses, QTc prolongation, adverse effects in elderly/demented</td>
</tr>
<tr>
<td>Olanzapine</td>
<td>IM (and even IV) option, less extrapyramidal, less QTc prolongation</td>
<td>Anticholinergic, half-life may be &gt;50 hours (older, female, nonsmoking, hepatic, renal), adverse effects in elderly/demented</td>
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</tbody>
</table>
Additional Considerations

- Hepatic/Renal status
- Obesity
- Other medications
- Age
- Dementia
- Tolerance/addiction

- It’s complicated: talk to a pharmacist if you’re not sure
  - Urgent situation: most of these agents are a fine choice for the short term. Later tweaks can be made with input from intensivist/pulmonologist/pharmacist
Level of Sedation

- **Ideal:** RASS 0 (awake, comfortable)
- **Goal:** RASS 0 to -2 (light sedation)

### Richmond Agitation-Sedation Scale (RASS)

<table>
<thead>
<tr>
<th>Score</th>
<th>Term</th>
<th>Description</th>
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<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 agitated</td>
<td>Pulls on or removes tubes or catheters, 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></td>
</tr>
<tr>
<td>-1</td>
<td>Drowsy</td>
<td>Not fully alert, sustained (&gt;10 seconds) awakening, eye contact to voice</td>
</tr>
<tr>
<td>-2</td>
<td>Light sedation</td>
<td>Briefly (&lt;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, 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>
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Level of Sedation

- Lighter sedation associated with fewer days of mechanical ventilation and lower incidence of tracheostomy
  - No effect on mortality, though
  - 2013 guidelines were RASS -2 (instead of current guideline of “0 to -2”), which led to over sedation and delay of improvement (unable to do therapy, etc.)

- Patient-centered:
  - Some patients require deeper sedation (even -4)
  - Others require none, even while vented

- Sedation goal can change
Covid-19 and Sedation

- Increased delirium and encephalopathy
  - Prominent agitation and confusion
  - Hyperreflexia
- Higher sedation requirements, especially right after intubation
  - UpToDate says:
    - General: RASS -1 to -2
    - Ventilator dyssynchrony: -2 to -3
    - Severe vent dyssynchrony and/or neuromuscular blockade: -4 to -5
- UpToDate: propofol and fentanyl generally preferred
  - Shortages may dictate choice
Monitoring

- **Scoring:** assess your goal according to the underlying problem(s) you’re treating
  - Pain scale for pain, RASS for sedation, CAM-ICU or ICDSC for delirium
- If you’re meeting your goal, back off to the lowest level that sustains the goal
Avoiding Over Sedation

- Infusions are associated with over sedation and increased mechanical ventilation days
  - Use lowest infusion rate that meets goal and lowest goal (e.g. RASS 0) that works for the patient
  - Use daily sedation interruption (DSI, “sedation holiday”)
- Or use intermittent boluses (protocolized) instead of an infusion
- On the other hand, some medications/patients exhibit tachyphylaxis, so doses may need to increase (although the RASS goal would not necessarily increase).
### 30870 SUP ICU Initiation of Mechanical Ventilation with Sedation Analgesia

#### Activity
- Head of Bed at 30 - 45 degrees
  - Unless contraindicated.

#### Nursing - Sedation Reduction
- **Sedation Reduction Protocol**
  - Protocol Document: \epics\Protocols\Sedation Reduction\Sedation Reduction Protocol September 2018.pdf
  - Assess and perform sedation reduction per sedation reduction protocol (refer to exclusion criteria on sedation reduction protocol).
- **Assessment and Parameters During Sedation Reduction**
  - Every 30 minutes and PRN to MAINTAIN the following parameters: Sedation Reduction Parameters: 1) Hemodynamic stability 2) Respiratory stability 3) ICP less than 15. 4) CPP greater than or equal to 60.
- **Resume Sedation - If Any One Sedation Reduction Parameter Not Maintained**
  - 1) Administer PRNs first before increasing infusion to achieve ordered RASS goal. 2) Follow sedation/analgesia infusion/bolus administration instructions.
- **Assess Level of Sedation While Patient on Sedating Medications**
  - Every 2 hours, and with bolus dose, or change in infusion dose, using RASS score.

#### Respiratory - Ventilator Settings
- **Mechanical Ventilation Settings**
  - CONTINUOUS, Mechanical ventilation settings: (35006) NOTE: Discontinue ventilator settings upon extubation or removal of the ventilator from the patient.
- **Capnography**

#### Respiratory - Weaning
- **Ventilator Weaning Protocol**
  - Assess and perform ventilator weaning per Ventilator Weaning Protocol (refer to exclusion criteria on ventilator weaning protocol; non-cardiac).
Medications

Choose medications from the Analgesia and Sedation sections, if indicated.

Narcotic Analgesics

- fentaNYL IV bolus and infusion
- HYDROmorphine (DILAUDID) IV bolus and infusion
- fentaNYL (SUBLIMAZE) IV ($)
  25-50 mcg, Intravenous, Q 30MIN PRN, Pain
- HYDROmorphine (PF) (DILAUDID) syringe 0.2-0.4 mg ($$)
  0.2-0.4 mg, Intravenous, Q 2H PRN, starting today at 1715, Until Discontinued, Pain, Routine

Sedation

- dexMEDeomidine (PRECEDEX) IV infusion ($$$)
  0-1.5 mcg/kg/hr, Intravenous, CONTINUOUS PRN, -Begin infusion at 0.4 mcg/kg/hr. -Titrato by 0.1 mcg/kg/hr every 30 minutes as needed to reach the desired RASS goal.
- propofol (DIPRIVAN) IV bolus, infusion and labs
- midazolam (VERSED) IV bolus and infusion - 2nd tier option
- LOrazepam (ATIVAN) IV bolus and infusion - 2nd tier option

Adjunctive Pain or Analgesia Agents

- ketamine (KETALAR) IV infusion ($$)
  0-400 mcg/kg/hr, Intravenous, CONTINUOUS PRN, -Begin infusion at 50 mcg/kg/hr. -Increase by 25 mcg/kg/hr every 5 minutes as needed to achieve analgesia or RASS goal.
Tapering

- Taper the opioid last
- Generally okay to abruptly discontinue sedation
  - If sedated >7 days with escalating doses due to tachyphylaxis, may need gradual taper (10-25% per day).
  - Consider chatting with an intensivist if sedated >7 days.
- Can see lipophilic accumulation with longer-term sedation (may take days to wake up)
- Daily sedation interruption helps with tapering
Withdrawal

- Occurs in maybe a third of patients sedated >7 days
- Higher doses of benzodiazepines or opioids associated with greater likelihood
- Monitor for symptoms of withdrawal and taper.
  - We’re used to doing this with alcohol withdrawal
Vasopressor Support

PUTTING THE SQUEEZE ON YOUR PATIENTS...
Etiology of shock

- Septic shock is less prevalent in Covid-19 than other causes of ARDS, but does occur
- Hypotension from sedation medications
- Cardiogenic shock

- Wuhan study: 35% required pressors (52 patients)
- New York: 95% of mechanically ventilated patients required pressors (130 patients).
  - Reason for difference unknown, but small numbers, probably different inclusion criteria, different interventions, different reporting
Indications for Vasopressors

- MAP <60 mmHg
- SBP drop >30 mmHg from baseline

- Treat underlying conditions first, or at least at the same time if it is an emergency
  - Especially hypovolemia. Pressors not adequately effective and more likely to injure a patient in a hypovolemic state.
  - But hypervolemia not helpful, especially in Covid-19
Vasopressor Rules

- One drug, many receptors
  - Multiple, sometimes conflicting effects
  - E.g. dobutamine. $\beta_{-1}$ increases cardiac output; $\beta_{-2}$ causes vasodilation

- Dose-response curve
  - Different actions (different affinity/activity for different receptors) at different doses
  - E.g. dopamine 2-10 mcg/kg/min $\beta_{-1}$ (cardiac); 10+ $\alpha$ (vasoconstriction)

- Direct actions vs reflex effects
  - E.g. norepinephrine $\beta_{-1}$ adrenergic effect would cause tachycardia, but reflex resulting from MAP increase as a result of $\alpha$ activity causes a stable or slightly reduced heart rate
Vasopressor Agents

- Norepinephrine
  - α-1, β-1. Strong vasoconstriction, modest increase in cardiac output
  - Preferred agent in septic shock

- Vasopressin
  - No mortality benefit when studied, but reduced required dose of norepinephrine. Might reduce need for renal replacement therapy.
  - Not a first-line agent
  - Fixed dose (0.04 u/min) except when titrating off (to avoid reflex hypotension)
Vasopressor Agents

- Phenylephrine
  - Pure $\alpha$ agonist
  - In theory should decrease cardiac output by increasing afterload, but in practice this doesn’t happen in the absence of preexisting cardiac dysfunction
Vasopressor Agents

- Dopamine
  - 1-2 mcg/kg/min: D-1 receptor action causes selective vasodilation, possibly increased blood flow to vital organs. Might actually get a reduction in MAP.
  - 5-10: β-1 activity increases cardiac output. Mostly increased stroke volume, some increased heart rate. A little α activity. Overall an increase in MAP.
  - >10: mostly α vasoconstriction, but weaker than norepinephrine. β effects limit dose in many patients because of tachy- and other dysrhythmias.
- Dose ranges above are theoretical. Actual volume of distribution and resulting concentration of drug in a given patient vary widely.
  - Start at 2 mcg/kg/min and titrate up to the desired effect, but be aware of the dose-response issues.
Less Commonly Used

- **Epinephrine**
  - Strong β-1, moderate β-2 and α-1
  - At low doses, increases cardiac output with minimal effect on MAP. At higher doses, the α effect predominates.
  - Mostly for anaphylaxis and post cardiac surgery. Occasionally for sepsis.

- **Dobutamine**
  - Inotrope, not pressor. Actually causes vasodilation.
  - Primarily used in cardiogenic shock. Not a good choice for sepsis.
Norepinephrine is widely used as a first choice for vasopressor support.
- For sedation hypotension, consider whether you can change sedation.
- Phenylephrine seems to be more readily available or at least more readily used in emergency, non-code situations (rapid response).
  - Okay to stabilize and switch to norepinephrine when able.
- Generally add vasopressin as a second pressor.
- No evidence in favor of 3+ pressors, but commonly done.
  - Phenylephrine vs. dopamine.
  - Consider chatting with an intensivist, especially if you’re considering a fourth.
Cardiogenic Shock

- Much more complex management, including potential mechanical interventions
- Norepinephrine preferred over dopamine
  - Higher mortality, dysrhythmia with dopamine
- If cardiogenic shock is felt to be primary driver, start norepinephrine to stabilize the patient and call intensivist and heart failure cardiologist
Complications

- Hypoperfusion from excessive vasoconstriction
  - Often in the setting of low cardiac output or hypovolemia
  - However, adequate MAP is more protective of kidneys and mesenteric organs than vasoconstriction is harmful, so don’t opt for severe hypotension even with evidence of localized perfusion compromise.
  - Talk to an intensivist if you get over this barrel

- Dysrhythmias
  - Sinus tach, afib, AVNRT, VT
  - Especially with dopamine
  - Adequate hydration helps
  - Often limits dose or requires a switch of agent
Complications

- MI
  - Increased myocardial demand > degree of coronary vasodilation
  - Avoid tachydyssrhythmias

- Extravasation
  - Local necrosis can be devastating
  - There isn’t really a “safer” pressor to use peripherally
  - Switch to a central line ASAP

- Hyperglycemia
  - Reduced insulin secretion, more with norepinephrine
  - You’re going to be watching for this anyway


