ICU Best Practices, Sedation, Pressors

BRENT J. RYAN, MD MPH

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

ABCDEF,

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

Table. ABCDEF Bundle

A	Assess, prevent, and manage pain
B	Both spontaneous awakening & breathing trials
C	Choice of medication management
D	Delirium
E	Early mobility & exercise
F	Family engagement and empowerment

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

ANW Intensivists Notes

Critical Care Best Practices

Assess/prevent/manage pain:	{Analgesia:35486}
Both spontaneous awakening and breathing trials?:	{SAT and SBT:35487}
Choice of analgesia & sedation:	{Choice of Sedation:35488}
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:	{

.INTENSIVISTPROG

.ICUBESTPRACTICES

.INTENSIVISTHPCONSULT

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
Thromboprophylaxis:	Chemical Mechanical
VAP prophylaxis:	HOB > 30 degrees and chlorhexidine
Gastric acid suppression (if intubated or home Rx):	H2 antagonist
Glycemic control:	Insulin infusion
Bowel regimen ordered (last BM: 5/12):	Yes
Line/device assessment:	Reviewed & no changes

Sedation

MILK OF AMNESIA AND OTHER TREATS…

Sedation – Why?

- Distress usually presents as 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 over sedation, 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.

Agent	Advantages	Disadvantages
Fentanyl (*not an amnestic*)	Strong analgesia, strong sedation, immediate onset, less hypotension	Lipophilic accumulation
Propofol (*not an analgesic*)	Strong sedation, immediate onset, rapid awakening (when used short-term), no hepatic or renal adjustments, little interaction, easy to titrate, antiepileptic	Hypotension, bradycardia, respiratory depression, lipophilic accumulation (debated)
Ketamine (*not an amnestic*)	Dissociative analgesic, maintains blood pressure, +/- reduced opioid tolerance	Off label use, increased sympathetic tone, hallucinations, delirium
Dexmedetomidine (central alpha-2 agonist)	Sedative sympatholytic, moderate anxiolysis and analgesia, may cause less delirium, may reduce vent days	Hypotension, hypertension, bradycardia (may persist after drug stopped)
Midazolam	Strong amnestic and anxiolytic, immediate onset, short duration (when used short-term)	Active metabolites accumulate in long-term use, lipophilic accumulation delirium, interactions
Haloperidol	Moderately sedating, minimal effect on vitals, IV formulation	Increasing half-life with additional doses, QTc prolongation, adverse effects in elderly/demented
Olanzapine	IM (and even IV) option, less extrapyramidal, less QTc prolongation	Anticholinergic, half-life may be >50 hours (older, female, nonsmoking, hepatic, renal), adverse effects in elderly/demented

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)

Score	Term	Description
+4	Combative	Overtly combative or violent, immediate danger to staff
+3	Very agitated	Pulls on or removes tubes or catheters, aggressive behavior toward staff
+2	Agitated	Frequent nonpurposeful movement or patient-ventilator dyssynchrony
+1	Restless	Anxious or apprehensive but movements not aggressive or vigorous
0	Alert and calm	
-1	Drowsy	Not fully alert, sustained (>10 seconds) awakening, eye contact to voice
-2	Light sedation	Briefly (<10 seconds) awakens with eye contact to voice
-3	Moderate sedation	Any movement (but no eye contact) to voice
-4	Deep sedation	No response to voice, any movement to physical stimulation
-5	Unarousable	No response to voice or physical stimulation

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

- [x] Sedation Reduction Protocol
  Protocol Document: \\epicfs01\epic$\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).
- [x] Assessment and Parameters During Sedation Reduction
  Every 30 minutes and PRN to MAINTAIN the following paramenters: Sedation Reduction Parameters: 1) Hemodynamic stability 2) Respiratory stability 3) ICP less than 15. 4) CPP greater than or equal to 60.
- [x] 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.
- [x] 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

- [x] Ventilator Weaning Protocol
  Protocol Document: \\epicfs01\epic$\Protocols\Vent Weaning\Mechanical Vent Weaning Protocol September 2018.pdf
  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
- ○ HYDROmorphone (DILAUDID) IV bolus and infusion
- ○ fentaNYL (SUBLIMAZE) IV ($)
  25-50 mcg, Intravenous, Q 30MIN PRN, Pain
- ◉ HYDROmorphone (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

- ○ dexMEDEtomidine (PRECEDEX) IV infusion ($$$)
  0-1.5 mcg/kg/hr, Intravenous, CONTINUOUS PRN, -Begin infusion at 0.4 mcg/kg/hr. -Titrate 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. β-1 increases cardiac output; β-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 β-1 (cardiac); 10+ α (vasoconstriction)
- Direct actions vs reflex effects
  - E.g. norepinephrine β-1 adrenergic effect would cause tachycardia, but reflex resulting from MAP increase as a result of α 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 α 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.

General Guidance – Sepsis or Sedation Hypotension

- 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 tachydysrhythmias
- 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

References

Anesi G. “Coronavirus disease 2019 (COVID-19): Critical care and airway management issues”. *UpToDate*. Accessed 05/18/20.

Fuchs B, Bellamy C. “Sedative-analgesic medications in critically ill adults: Selection, initiation, maintenance, and withdrawal”. *UpToDate*. Accessed 05/18/20.

Manaker, S. “Use of vasopressors and inotropes”. *UpToDate*. Accessed 05/18/20.

Mikkelsen ME, Netzer G, Iwashyna T. “Post-intensive care syndrome (PICS)”. *UpToDate*. Accessed 05/18/20.

Tietze KJ, Fuchs B. “Sedative-analgesic medications in critically ill adults: Properties, dosage regimens, and adverse effects”. *UpToDate*. Accessed 05/18/20.