Sedation and Mobility in the ICU

What is the Evidence?

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Outline

- Sedation in ICU
  - Purpose/Goals
  - Common Drugs
  - Sedation delivery strategies
- Mobility in the ICU
  - Weakness with critical illness
  - Early Mobility studies
- Combining sedation strategies and Early Mobility in the ICU
ICU can be a frightening place....
Etiology of Agitation

**PEOPLE**
- Family
- RN
- House Staff
- Attending Physicians
- Consultants
- RT
- PT
- Pharmacist
- Radiology Techs
- Others (eg, IT)

**ENVIRONMENTAL & OTHER**
- Lighting
- Noise
- Temperature
- Windows
- Routine Care Times
- Visiting Hours
- Departmental/Hospital Policies
- Regulatory Policies
- Other

**PATIENT FACTORS**
- Age & Sex
- PM History
- Diagnosis/Operations
- Allergies
- Drug Reaction History
- ETOH & Drug Abuse
- Severity of Illness
- Exam
- Other

**DRUGS & DEVICES**
- Sedatives
- Analgesics
- NM Blockers
- Drug Side Effects
- Drug-Drug Interactions
- ET Tubes
- Tracheotomy Tubes
- Nasogastric Tubes
- Feeding Tubes
- Foley Catheters
- PA, CV & Art. Lines
- Restraints
- Other

**TECHNOLOGY**
- Computer Hardware & Software
- Laboratory
- Radiology
- Std Bedside Monitors
- BIS
- Lack of sleep
- Ventilator
- Other

**MEASURES, PROCESS TOOLS & COMMUNICATION**
- Lab * XRAY Results
- Radiology Results
- Progress Notes
- Orders
- Flow sheet/Monitor Data
- Scoring Systems
- Diagnostic Tools
- Pagers, Phones, E-mail
- Rounds
- Protocols
- Outcomes
Etiology of Agitation

Pain
An unpleasant sensation as a consequence of injury, disease, or emotional disorder

Anxiety
A sustained state of apprehension and autonomic arousal in response to real or perceived threats

Confusion
Disturbance of consciousness characterized by an acute onset and fluctuation course of impaired cognitive functioning (impaired ability to receive, process, store and recall information)

Agitation

Delirium
Indications for Sedative and Analgesia

- Pain
- Anxiety
- Facilitate patient care
- Amnesia
- Decrease oxygen consumption
Negative consequences of Agitation and treatment of Agitation

- Self – Extubation
- Self removal of lines
- Increased systemic and myocardial oxygen consumption
- Failure to participate with therapeutic interventions

- Increased ICU/hospital stays
- Increased time on ventilator
- Increased delirium
- Increased VAP
- Difficult neurologic assessments
- Long term psychological problems
Lorazepam and Delirium

Fig. 1. Lorazepam and the probability of transitioning to delirium. The probability of transitioning to delirium increased with the dose of lorazepam administered in the previous 24 h. This incremental risk was large at low doses and plateaued at around 20 mg/day.
Impact of Delirium on ICU Patients

- Delirium present in 60 to 80% of ICU patients
- Most common onset was 2 to 3 days post admission
- Average delirium duration was 3.4 +/- 1.9 days
- Measuring Delirium
  - CAM ICU
  - Delirium Screening Checklist
- Duration of Delirium significantly associated with increased hospital LOS (r=0.68, P=0.006) *Corrected for severity of illness

Psychological Burden following Critical Illness

- Irritability, social isolation, Depression, Anxiety, PTSD
- Complex problem, limited studies
- Appears that:
  - More common if uncontrolled pain, anxiety
  - Ability to recall factual information may be protective
Indications for Sedative and Analgesia

- Pain
- Anxiety
- Facilitate patient care
- Amnesia
- Decrease oxygen consumption

HOW MUCH?
Goals of Sedation / Analgesia

  - *Patients should ideally be “detached from the ICU environment”*

- 1987: Bion, Int Care Medicine 1987:13;215
  - *Patients should be “asleep but easily arousable”*

- 2008 to present: To have patients who are
  - *Pain and anxiety-free*
  - *Cooperative and accepting of care*
  - *Amnesia not always necessary*
Common medications used in the ICU
### Sedatives

#### Benzodiazepines

- Sedative, anxiolytic, amnestic, opioid sparing

<table>
<thead>
<tr>
<th>Agent</th>
<th>Lipid Soluble</th>
<th>Time to onset</th>
<th>Half-Life (hours)</th>
<th>Cost</th>
<th>Side Effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>Midazolam</td>
<td>+++</td>
<td>2-5 min</td>
<td>3-11</td>
<td>6mg/hr $65-$309</td>
<td>Unpredictable waking with long continuous infusion</td>
</tr>
<tr>
<td>Lorazepam</td>
<td></td>
<td>5-20 min</td>
<td>8-15</td>
<td>48 mg/day $55.00</td>
<td>Solvent related Acidosis/RF in high dose Precipitation in tubing</td>
</tr>
<tr>
<td>Diazepam</td>
<td>+++</td>
<td>2-5 min</td>
<td>20-120</td>
<td>20mg / 4hr $5-20.50</td>
<td>Phelbitis</td>
</tr>
</tbody>
</table>
Sedatives

Propofol

- Sedative
- Short onset and duration of action
  - 1-2 minute onset
  - 2-8 minutes duration
- Sedation when frequent neurologic assessment is needed
- Adverse Events:
  - Hypotension
  - Elevated Triglycerides
  - Propofol Syndrome
Sedatives

Ketamine

- NMDA receptor antagonist
- “Dissociative anesthesia”
- Sedative and analgesic properties

Side Effects:
- Hallucinations
- Bronchodilation
- Hypertension
Sedatives

Alpha 2 receptor agonist

- Sedative, Anxiolysis, analgesic-sparing qualities

Clonidine
- Antihypertensive
- Anxiolytic and analgesic-sparing properties

Dexametomidine
- New medication; not currently available in Canada
- Deeply sedated but able to perform complex tasks
- Side Effects: Bradycardia, hypotension
Analgesics
Narcotics

- Mainly analgesia, mild anxiolytic properties
- Relieves dyspnea, coughing

Side Effects:
- Delirium
- Impairs gut mobility; constipation, not tolerating tube feeds
- Respiratory depressant
## Analgesics

### Narcotics

<table>
<thead>
<tr>
<th>Drug</th>
<th>Lipid Soluable</th>
<th>Time to Onset</th>
<th>Duration of Action</th>
<th>Drug Elimination</th>
<th>Comments</th>
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<tr>
<td>Morphine</td>
<td>-</td>
<td>5 – 10 min</td>
<td>4 hrs</td>
<td>Liver then kidney</td>
<td></td>
</tr>
<tr>
<td>Fentanyl</td>
<td>+++</td>
<td>1 – 2 min</td>
<td>0.5 – 1 hr</td>
<td>Liver</td>
<td>With long durations of infusions can have prolonged effect</td>
</tr>
<tr>
<td>Hydromorphone</td>
<td>-</td>
<td>5-10min</td>
<td>4 hrs</td>
<td>Liver then Kidney</td>
<td>Preferred to morphine in renal failure</td>
</tr>
<tr>
<td>Remifentanil</td>
<td>++++</td>
<td>1 min</td>
<td>20 min</td>
<td>Blood/tissue esterase</td>
<td>$$</td>
</tr>
<tr>
<td>Meperidine</td>
<td>+</td>
<td>3 – 5 min</td>
<td>1 – 4 hrs</td>
<td>Liver then kidney</td>
<td>Seizures</td>
</tr>
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Analgesics

- To avoid complications associated with narcotics, consider the addition or substitution with non-narcotic analgesia:
  - Acetaminophen
  - Non-Steroidal Analgesic
  - Epidural with local anesthetic
  - Nerve Blocks
  - Tricyclic antidepressants (Neuropathic pain)
Neuroleptics

- Dopamine antagonists
- Treatment of psychosis, delirium
- Typical antipsychotics: Haloperidol
- Atypical antipsychotics: Olanzapine, Quetiapine

Side Effects:
- Extrapyradimal side effects: Tardive dyskinesia, dystonias, parkinsonism
- Prolonged QT
Strategies to optimize sedation delivery in the ICU

- Sedation Scales
- Sedation protocols
- Daily Sedation interruption trials
- New Generation Medications
Factors Affecting Sedation Titration

- Nursing Attitudes and beliefs about critical illness
- Family member’s perception of agitation
- Nursing workload and staffing ratios

### 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 nonpurposeful movement, fights ventilator</td>
</tr>
<tr>
<td>+1</td>
<td>Restless</td>
<td>Anxious 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, but has sustained awakening (eye opening/eye contact) to voice (&gt;10 seconds)</td>
</tr>
<tr>
<td>−2</td>
<td>Light sedation</td>
<td>Briefly awakens with eye contact to voice (&lt;10 seconds)</td>
</tr>
<tr>
<td>−3</td>
<td>Moderate sedation</td>
<td>Movement or eye opening to voice (but no eye contact)</td>
</tr>
<tr>
<td>−4</td>
<td>Deep sedation</td>
<td>No response to voice, but movement or eye opening to physical stimulation</td>
</tr>
<tr>
<td>−5</td>
<td>Unarousable</td>
<td>No response to voice or physical stimulation</td>
</tr>
</tbody>
</table>

**Procedure for RASS Assessment**

1. Observe patient
   - Patient is alert, restless, or agitated. Score 0 to +4
2. If not alert, state patient’s name and say to open eyes and look at speaker.
   - Patient awakens with sustained eye opening and eye contact. Score −1
   - Patient awakens with eye opening and eye contact, but not sustained. Score −2
   - Patient has any movement in response to voice but no eye contact. Score −3
3. When no response to verbal stimulation, physically stimulate patient by shaking shoulder and/or rubbing sternum.
   - Patient has any movement to physical stimulation. Score −4
   - Patient has no response to any stimulation. Score −5

Adapted with permission.20
Nurse directed Sedation Protocol

1. Sedation needed: target to Ramsay score 3.
2. Exclude reversible causes of agitation.
3. Is pain likely?

Yes → Fentanyl 25–50 μg every 5 mins until pain/agitation relieved.

No → Morphine 1–5 mg up to every 2 hrs.

Is agitation causing acute deterioration (e.g., hypoxia, high peak airway pressures) necessitating immediate control?

Yes → Requiring fentanyl bolus > every 2 hrs.

No → Fentanyl infusion 25–100 μg/hr.

Decrease fentanyl infusion by 25 μg/hr or lorazepam infusion by 0.25 mg/hr every 4 hrs until infusion discontinued.

Yes → Lorazepam infusion 0.5–1 mg/hr.

No → Targeted sedation achieved.

Reassess sedation regimen and Ramsay score every 4 hrs.

Yes → Rebolus and increase fentanyl infusion by 25 μg/hr and/or rebolus and increase lorazepam infusion by 0.25 mg/hr.

No → Lorazepam 1–4 mg up to every 2 hrs.

Rebolus and increase lorazepam infusion by 0.25 mg/hr.
Results

- Randomized trial comparing protocol sedation (162) versus traditional sedation orders by physician (n=159)

<table>
<thead>
<tr>
<th>Days</th>
<th>Traditional Sedation</th>
<th>Protocol Sedation</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Continous IV sedation</td>
<td>6.4</td>
<td>3.5</td>
<td>0.003</td>
</tr>
<tr>
<td>Mechanical Ventilation</td>
<td>4.9</td>
<td>2.3</td>
<td>0.008</td>
</tr>
<tr>
<td>ICU LOS</td>
<td>7.5</td>
<td>5.7</td>
<td>0.003</td>
</tr>
<tr>
<td>Hospital LOS</td>
<td>19</td>
<td>14</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Tracheostomy Rates 6.2% with protocol sedation versus 13.2% with traditional doctor orders (p=0.04)
Daily Sedation Interruption


- 128 pts ventilated >48 hours in ICU randomized to:
  - Daily Sedation Awakening Trial (SAT)
  - Traditional Sedation; titrated to goal sedation score

- Daily Sedation Awakening Trial:
  - Daily Interruption of infusions (sedative/narcotic) followed by assessment
  - If awake and following commands ➔ Infusion d/c’ed
  - If agitated ➔ Infusion resumed at 50% dose initially then titrated to goal level of sedation
Outcomes

Average Cumulative Sedative Dose was lower with SAT:
Midazolam 230 mg vs 425 mg (p = 0.05)
Morphine 205 mg vs 480 mg (p = 0.01)
Propofol 15,200 mg vs 17,600 mg (p = NS)

Average Cumulative Sedative Dose was lower with SAT:
Midazolam 230 mg vs 425 mg (p = 0.05)
Morphine 205 mg vs 480 mg (p = 0.01)
Propofol 15,200 mg vs 17,600 mg (p = NS)

New Generation medications
Dexmedetomidine

![Forest plot showing the incidence of delirium in 4 randomized studies that compared dexmedetomidine with midazolam or propofol after cardiac surgery, with lorazepam, with midazolam, or with standard care. The cumulative odds ratio shows a dramatic reduction (0.45) of delirium with dexmedetomidine use. (Data from Refs. 38, 44, 45, 46)](chart.png)

However in the real world....

Despite this evidence, sedation protocols and daily awakening are not widely used in daily practice
Interventions paired with Daily Sedation Interruptions

- Spontaneous Breathing Trials
- Early Mobility
Wake up and Breathe

All patients received Spontaneous breathing trials
Randomized to daily sedation interruption vs. traditional sedation


Other findings associated with DSI:
• Increase in self-extubation
  (10% vs 4%, p = 0.03)
• Decrease in 1 year mortality
  (44% vs 58%, p = 0.01)
Bed rest In Critical Illness

Complications:

- Skeletal muscle atrophy and weakness
- Joint contractures
- Thromboembolic disease
- Insulin resistance
- Microvascular dysfunction
- Atelectasis
- Pressure ulcers

Theoretical Advantage:

- Conserve metabolic resources for utilization for healing and recovery
- Reduce oxygen consumption by muscles; divert O₂ delivery toward injured tissues and organs needing more oxygen
- Reduce requirements for ventilation and high FiO₂
- Improve blood flow to the CNS
- Reduce harmful inflammation
- Reduce stress on the heart
- Avoid pain from and additional injury to an injured body part

### Weakness associated with Critical Illness

#### Weakness 2° Deconditioning
- Common
- Mechanical unloading of muscles causes atrophy.
- Bed rest associated with loss of muscle mass 1% to 2.5% per day
- Weakness can be demonstrated after 1 – 2 days of Mechanical ventilation

#### ICU Acquired Weakness (ICUAW)
- AKA: ICU neuropathy/myopathy
- Nerve and muscle dysfunction due to:
  - Mechanical unloading
  - Inflammation
  - Oxidative stress
  - Nutritional deficits
- May take months to reverse
Risk Factors for ICU acquired Weakness

- Multisystem Organ Dysfunction
- Immobility
- Hyperglycemia
- Use of steroids and Neuromuscular blockers

Canadian cohort study of 109 ARDS survivors for 1 year

- Median age: 45
- Median APACHE II: 23
- Median ICU los: 25 days
Good recovery of pulmonary function

Diffusion capacity only finding on PFT that remained impaired at 1 year.

- 6 minute walk distance limited by neuromuscular complaints
Global Assessment at one year

- 49% back to work at a year
- Most back to baseline weight
- **All** patients described poor function due to weakness, fatigue and loss of muscle bulk
- Specifically:
  - Chronic pain from Chest tube sites (12%)
  - Entrapment neuropathies (7%)
  - Immobility of large joints due to hypertrophic ossification (5%)
  - Tracheostomy scars bothersome – OR to revise (7%)
  - Contractured fingers or frozen shoulders (4%)
  - Tracheal stenosis needing OR (2%)
Early Mobility

Can we prevent muscle weakness associated with critical illness with physiotherapy/exercise?

- Pairing with Sedation Awakening Trials
- Small observational studies
- Randomized Control Trials
<table>
<thead>
<tr>
<th>LEVEL</th>
<th>Status</th>
<th>MT: Passive ROM 3x/d</th>
<th>MT: q2Hr turning</th>
<th>Active Resistance PT</th>
<th>Sitting Position Minimum 20 minutes 3x/d</th>
<th>Can move arm against gravity</th>
<th>Sitting on edge of bed PT + MT</th>
<th>Can move leg against gravity</th>
<th>Sitting on edge of bed PT + MT</th>
<th>Active Transfer to Chair (OOB) PT + MT Minimum 20 minutes/d</th>
</tr>
</thead>
<tbody>
<tr>
<td>LEVEL I</td>
<td>Unconscious</td>
<td>MT: Passive ROM 3x/d</td>
<td>q2Hr turning</td>
<td>Active Resistance PT</td>
<td>Sitting Position Minimum 20 minutes 3x/d</td>
<td>Can move arm against gravity</td>
<td>Sitting on edge of bed PT + MT</td>
<td>Can move leg against gravity</td>
<td>Sitting on edge of bed PT + MT</td>
<td>Active Transfer to Chair (OOB) PT + MT Minimum 20 minutes/d</td>
</tr>
<tr>
<td>LEVEL II</td>
<td>Conscious</td>
<td>Passive ROM 3x/d</td>
<td>q2Hr turning</td>
<td>Active Resistance PT</td>
<td>Sitting Position Minimum 20 minutes 3x/d</td>
<td>Can move arm against gravity</td>
<td>Sitting on edge of bed PT + MT</td>
<td>Can move leg against gravity</td>
<td>Sitting on edge of bed PT + MT</td>
<td>Active Transfer to Chair (OOB) PT + MT Minimum 20 minutes/d</td>
</tr>
<tr>
<td>LEVEL III</td>
<td>Conscious</td>
<td>Passive ROM 3x/d</td>
<td>q2Hr turning</td>
<td>Active Resistance PT</td>
<td>Sitting Position Minimum 20 minutes 3x/d</td>
<td>Can move arm against gravity</td>
<td>Sitting on edge of bed PT + MT</td>
<td>Can move leg against gravity</td>
<td>Sitting on edge of bed PT + MT</td>
<td>Active Transfer to Chair (OOB) PT + MT Minimum 20 minutes/d</td>
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<tr>
<td>LEVEL IV</td>
<td>Conscious</td>
<td>Passive ROM 3x/d</td>
<td>q2Hr turning</td>
<td>Active Resistance PT</td>
<td>Sitting Position Minimum 20 minutes 3x/d</td>
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**CCM 2008;36: 2238-2243**
Outcomes

Early Mobility

- Days to first out of bed: Usual Care (11.3) vs. Early mobility (5), $P<0.001$
- Ventilator Days: Usual Care (9) vs. Early mobility (7.9), $P=0.16$
- ICU LOS: Usual Care (6.9) vs. Early mobility (5.5), $P<0.01$
- Hospital LOS: Usual Care (14.5) vs. Early mobility (11.2), $P=0.02$

• All outcomes adjusted for severity of illness
• All patients had daily SAT/SBT

CCM 2008;36: 2238- 2243
Early Mobility in ICU

- Sedated 104 MV patients; Prospective randomized trial
- Both groups had sedation protocol with daily SAT/ SBT

<table>
<thead>
<tr>
<th></th>
<th>Days with delirium</th>
<th>Duration of Mechanical Ventilation</th>
<th>ICU LOS</th>
<th>Hospital LOS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Traditional</td>
<td>4</td>
<td>6.1</td>
<td>7.9</td>
<td>13.5</td>
</tr>
<tr>
<td>Early Mobility</td>
<td>2</td>
<td>3.4</td>
<td>5.9</td>
<td>12.9</td>
</tr>
</tbody>
</table>

P = 0.02
P = 0.02
P = 0.08
P = 0.9

Lancet 2009; 373: 1874-82.
Early Mobility in ICU
More functional independence at hospital discharge

Lancet 2009; 373: 1874-82.
Over sedation and Immobility

- Over sedation
  - Anxiety
  - Weakness, Prolonged Wean
  - Delirium

- Immobility
  - Inability to cooperate with physio
  - Feeling a lack of control
  - Pain associated with immobility

↓ Ability to move
VAP
Over sedation and Immobility

An Awake Patient
Free of pain and anxiety

Early Mobility

Able to cooperate with physio

Prevent ICU AW
Optimize wean from ventilator

↓ Anxiety

Sense of control
Changing Sedation/Mobility Paradigm in the ICU

Barriers to overcome:

- ICU Culture (Focus on survival)
- Medical beliefs regarding therapeutic nature of bedrest/sedation/suffering
- Resources
- Logistics
- Concerns of safety
Changing Paradigm of Sedation/Mobility in the ICU
Conclusions

- Long term psychological and neuromuscular consequences of critical illness is common.
- Sedations strategies including sedation protocols and daily interruption of sedation are effective in decreasing lengths of stay, tracheostomy rates and delirium in ICU.
- Mobilizing patients early in ICU associated with shorter stays and improved function at hospital discharge.