Agitated patient in ICU-approach & management

Arjun Srinivasan
Agitation

- Extreme arousal, irritability, excess motor activity driven by internal sense of discomfort such as disease, pain, anxiety and delirium

- Acute

- Ongoing
Why bother?

- Harm to self & staff
- Prolonged & inadequate ventilation
- Inappropriate & overuse of sedation
- Increased ICU cost, morbidity & mortality
Approach

• Onset & organ dysfunction

• Etiology & reversibility

• Therapy
Etiology

Potentially Life Threatening
- Gas Exchange: hypoxemia, hypercarbia
- Metabolic: hypoglycemia, acidosis
- Ventilator Related: endotracheal tube malposition, tension pneumothorax
- Infection: central nervous system infection, sepsis
- Drug and Alcohol Related: intoxication, withdrawal syndromes
- Ischemia: myocardial, intestinal, corobral
- Miscellaneous: abdominal compartment syndrome, hypotension/poor perfusion

Non Immediately Life Threatening
- Ventilator dysynchrony
- Inadequate flow rates
- Too low/high tidal volumes
- Uncomfortable body position
- Discomfort from kinked or tugging catheters
- Fear/Anxiety
- Pain
- Itch
- Inability to communicate
- Sleep deprivation
- Full bladder
- Need to defecate
- Nausea
- Nicotine withdrawal
- Dry mouth
- Delirium and drug side-effects
- Paradoxical reaction to benzodiazepines, anticholinergics

Physical distress
Psychological distress

AGITATION

Shyoko Honiden and Mark D. Siegel
Ventilator dyssynchrony

Agitation
Patient ventilator dyssynchrony

• Ventilator should cycle in synchrony with pt’s respiratory drive
• Indirectly proportional degree of support
• Dyssynchrony arises frequently
  – Trigger
  – Rest of inspiration (flow dependent)
  – Cycle
  – End of expiration
Physical signs

**Failed trigger**
- Chest wall & abdominal effort in spite of no breath delivery

**Trigger delay**
- Appreciable delay between effort & breath delivery

**PEEPi**
- Inward chest wall movement persisting up to next inspiration
- Audible expiratory sound during next inspiration
Trigger dyssynchrony

• Too little
  – Inappropriate setting
  – Dynamic hyperinflation & PEEPi
  – Decreased effort / drive
  – Increased resistance (ET tube / tubing / pt’s respiratory mechanics)

• Time delay
  – Ventilator design anomaly

• Too much
  – Inappropriate setting
  – Water / secretions in tubing
  – Leak / expiratory valve fault
## Strategies for Optimizing trigger synchrony

<table>
<thead>
<tr>
<th>Manifestation</th>
<th>Cause</th>
<th>Treatment</th>
<th>Potential Consequences</th>
</tr>
</thead>
<tbody>
<tr>
<td>Trigger dyssynchrony (including untriggered breaths)</td>
<td>Intrinsic positive end-expiratory pressure (PEEP&lt;sub&gt;i&lt;/sub&gt;) (dynamic hyperinflation, DH)</td>
<td>Treat airflow obstruction</td>
<td>May not work in spontaneously breathing patient</td>
</tr>
<tr>
<td></td>
<td></td>
<td>↓ Minute ventilation (V&lt;sub&gt;E&lt;/sub&gt;)</td>
<td>May lead to ↑ RR</td>
</tr>
<tr>
<td></td>
<td></td>
<td>↑ Inspiratory flow rate (IFR)</td>
<td>If PEEP&lt;sub&gt;E&lt;/sub&gt; &gt; 85% PEEP&lt;sub&gt;i&lt;/sub&gt;, DH may worsen</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Add extrinsic PEEP</td>
<td></td>
</tr>
<tr>
<td>Improper trigger sensitivity</td>
<td></td>
<td>Decrease trigger pressure to 0.5–1.0 cmH&lt;sub&gt;2&lt;/sub&gt;O</td>
<td>Autocycling</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Δ to FT or ↑ Flow sensitivity</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Minimize sedation</td>
<td></td>
</tr>
<tr>
<td>↓ Respiratory drive</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Respiratory muscle weakness</td>
<td></td>
<td>Correct electrolytes, nutrition</td>
<td></td>
</tr>
<tr>
<td>↑ Endotracheal tube resistance</td>
<td></td>
<td>Δ Endotracheal tube</td>
<td></td>
</tr>
</tbody>
</table>
Flow dyssynchrony

• Frequently due to low fixed flow setting in volume cycled flow controlled ventilation
• Pt has breath to breath variability
• Mismatch especially in cases of ARDS & COPD
• Patient’s requirement may exceed set parameters
  – Minute ventilation
  – Tidal volume
  – Hypoxemia
  – Flow rate
• Elicits sensation of dyspnea & increases WOB
“Pulled down” pressure tracing

Current Opinion in Critical Care 2010, 16:261–268
Strategies for optimizing flow synchrony

• Increase flow rate
  – Pros
    • Decreases inspiratory time
    • Allows more expiratory time
    • Decreases dynamic hyperinflation & PEEPi
  – Cons
    • Increases PIP
    • Causes tachypnea

• Increase MVe & TV
  – Not always possible

• Decrease CO2 production
  – Treating fever & sepsis
Cycle dyssynchrony

• **Cycling**
  – Parameter determining the switch from inspiration to expiration
  – It is volume / time in ACMV & flow in PSV

• **Synchrony**
  – Patient’s Ti (neural Ti) = machine Ti

• **Dyssynchrony**
  – Neural Ti > machine Ti or neural Ti < machine Ti
Does cycle dyssynchrony occur in PSV?

• Usually no

• Can occur in presence of severe obstruction
  – Ventilators use flow for cycling in PSV
  – Usually < 25% of PF or 5 Ltrs/min
  – Rate of decrease of flow is slow & inspiratory time prolonged

• Tackled by
  – Increasing inspiratory rise time % or changing cycling parameters
  – Decreasing PS (may increase WOB)
Last difficult to ventilate pt needed....

- 18 days of ventilation

- ~ 5 grams of midazolam

- ~ 12 grams of propofol

- ~ 4 grams of vecuronium

- ~ 200 mg of haloperidol

- ~ 100 mg of morphine
What if no cause is identified?

- Structured ICU sedation algorithm
- Target specified, patient focused
- Incorporating scales for assessing
  - Pain
  - Sedation need
  - Delirium
Pain

• Whether present?

• If yes, then why?

• Management
Whether present?

• Omnipresent
  – Day to day procedures (suctioning/dressing changes/turning)
  – Improper positioning
  – Immobilization
  – Full bladder
  – Post operative/wound site pain
  – Cardiac/visceral pain (constipation/ileus)
How to detect?

• Able to communicate
  – Verbal or non verbal localization
  – Quantification by appropriate scales
    • Visual analog scale
    • Numeric scales
    • Verbal descriptive rating

• Unable to communicate
  – Inferred by observable behaviors & vital parameters
  – Limited by lack of specificity
  – BPS & CPOT have been used and validated recently
# Behavioral Pain Scale Tool

<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>

Score of 3 = no pain & 12 = maximum pain
# Critical-Care Pain Observation Tool

<table>
<thead>
<tr>
<th>Indicator</th>
<th>Score</th>
<th>Operational definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Facial expressions</td>
<td>0</td>
<td>No muscle tension observed</td>
</tr>
<tr>
<td>Tense</td>
<td>1</td>
<td>Presence of frowning, brow lowering, orific tightening, and levator contraction, or any other change (e.g., opening eyes or tearing during nociceptive procedure)</td>
</tr>
<tr>
<td>Grimacing</td>
<td>2</td>
<td>All previous facial movements plus eyelid tightly closed (the patient may present with mouth open or biting the endotracheal tube)</td>
</tr>
<tr>
<td>Body movements</td>
<td>0</td>
<td>Does not move at all (doesn’t necessarily mean absence of pain) or normal position (movements not aimed toward the pain site or not made for the purpose of protection)</td>
</tr>
<tr>
<td>Protection</td>
<td>1</td>
<td>Slow, cautious movements, touching or rubbing the pain site, seeking attention through movements</td>
</tr>
<tr>
<td>Restlessness</td>
<td>2</td>
<td>Pulling tube, attempting to sit up, moving limbs/throwing, not following commands, striking at staff, trying to climb out of bed</td>
</tr>
<tr>
<td>Compliance with the ventilator (intubated patients)</td>
<td>0</td>
<td>Alarms not activated, easy ventilation</td>
</tr>
<tr>
<td>Tolerating ventilator or movement</td>
<td>1</td>
<td>Coughing, alarms may be activated but stop spontaneously</td>
</tr>
<tr>
<td>Fighting ventilator</td>
<td>2</td>
<td>Asynchrony: blocking ventilation, alarms frequently activated</td>
</tr>
<tr>
<td>Vocalization (extubated patients)</td>
<td>0</td>
<td>Talking in normal tone or no sound</td>
</tr>
<tr>
<td>Talking in normal tone or no sound</td>
<td>1</td>
<td>Sighing, moaning</td>
</tr>
<tr>
<td>Crying out, sobbing</td>
<td>2</td>
<td>Crying out, sobbing</td>
</tr>
<tr>
<td>Muscle tension: Evaluation by passive flexion and extension of upper limbs when patient is at rest or evaluation when patient is being turned</td>
<td>0</td>
<td>No resistance to passive movements</td>
</tr>
<tr>
<td>Relaxed</td>
<td>1</td>
<td>Resistance to passive movements</td>
</tr>
<tr>
<td>Tense, rigid</td>
<td>2</td>
<td>Strong resistance to passive movements, incapacity to complete them</td>
</tr>
<tr>
<td>Very tense or rigid</td>
<td></td>
<td></td>
</tr>
<tr>
<td>TOTAL</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Pain Management Nursing, Vol 11, No 2 (June), 2010: pp 115-125*
Agitation- sedation scales

- First used by Ramsay et al in 1974
- Titrate sedation – target specific end points
- Shown to decrease
  - Over sedation & costs
  - Dose of sedatives & analgesics
  - Duration of mechanical ventilation & early weaning
  - Nosocomial infections
Various scales in use

- Ramsay Sedation Scale (RSS)
- Richmond Agitation-Sedation Scale (RASS)
- Sedation Agitation Scale (SAS)
- Motor Activity Assessment Scale (MAAS)
- Adaptation to the Intensive Care Environment (ATICE) instrument
- Minnesota Sedation Assessment Tool (MSAT)
- Vancouver interaction and calmness scale (VICS)
Delirium

• Present in 35-80% of critically ill patients
• Independent predictor
  – longer hospital stay
  – Higher hospital costs
  – Higher mortality
• Not easily recognized by treating physicians
• Caused by interplay of multiple factors
Chemically

- Increased dopamine
- Decreased acetyl choline
- Serotonin imbalance
- Endorphin hyperactivity
IATROGENIC/ENVIRONMENTAL

- Sedative/analgesic use
-Immobilization (restraint, catheters)
-TPN
-Sleep deprivation
-Malnutrition
-Anemia (phlebotomy)

HOST FACTORS

- Underlying co-morbidities (liver, renal, diabetes, hypertension)
- Elderly
- Pre-existing cognitive impairment/dementia
- Hearing/vision impairment
- Neurologic disease (stroke, seizure)
- Alcoholism, smoking

ACUTE ILLNESS.

- Severe sepsis
- ARDS
- MODS
- Drug overdose/illicit drugs
- Nosocomial infection
- Metabolic disturbance

Delirium in the ICU
Can these scales be implemented?

Large-scale implementation of sedation and delirium monitoring in the intensive care unit: A report from two medical centers

Objective: To implement sedation and delirium monitoring via a process-improvement project in accordance with Society of Critical Care Medicine guidelines and to evaluate the challenges of modifying intensive care unit (ICU) organizational practice styles.

Design: Prospective observational cohort study.

Setting: The medical ICUs at two institutions: the Vanderbilt University Medical Center (VUMC) and a community Veterans Affairs hospital (York-VA).

Subjects: Seven hundred eleven patients admitted to the medical ICUs for >24 hrs and followed over 4,163 days during a 21-month study period.

Interventions: Unit-wide nursing documentation was changed to accommodate a sedation scale (Richmond Agitation-Sedation Scale) and delirium instrument (Confusion Assessment Method for the ICU). A 20-min introductory in-service was performed for all ICU nurses, followed by graded, staged educational interventions at regular intervals. Data were collected daily for compliance, and randomly 40% of nurses each day were chosen for accuracy spot-checks by reference raters. An implementation survey questionnaire was distributed at 6 months.

Measurements and Main Results: The implementation project involved 64 nurses (40 at VUMC and 24 at York-VA). Sedation and delirium monitoring data were recorded for 711 patients (614 at VUMC and 97 at York-VA). Compliance with the Richmond Agitation-Sedation Scale was 94.4% (21,331 of 23,220) at VUMC and 99.7% (5,387 of 5,403) at York-VA. Compliance with the Confusion Assessment Method for the ICU was 90% (7,323 of 8,166) at VUMC and 84% (1,571 of 1,871) at York-VA. The Confusion Assessment Method for the ICU was performed more often than requested on 63% of shifts (5,146 of 8,166) at VUMC and on 8% (151 of 1871) of shifts at York-VA. Overall weighted-κ between bedside nurses and reference raters for the Richmond Agitation-Sedation Scale were 0.89 (95% confidence interval, 0.88 to 0.92) at VUMC and 0.77 (95% confidence interval, 0.72 to 0.83) at York-VA. Overall agreement (κ) between bedside nurses and reference raters using the Confusion Assessment Method for the ICU was 0.92 (95% confidence interval, 0.90–0.94) at VUMC and 0.75 (95% confidence interval, 0.68–0.81) at York-VA. The two most-often-cited barriers to implementation were physician buy-in and time.

Conclusions: With minimal training, the compliance of bedside nurses using sedation and delirium instruments was excellent. Agreement of data from bedside nurses and a reference-standard rater was very high for both the sedation scale and the delirium assessment over the duration of this process-improvement project. (Crit Care Med 2005; 33:1199–1205)

Key Words: delirium; sedation; implementation; mechanical ventilation; protocols; monitoring; intensive care; nursing; quality improvement; process improvement; clinical practice guidelines
General measures

- Reassurance (for fear, anxiety)
- Writing board if unable to communicate
- Repositioning the patient
- Repositioning ET > 2 cms from carina
- Treatment of withdrawal state
- Correcting metabolic derangements
- Catheterization
- Music therapy
- Hypnosis
How drug use in ICU is different?

- Advanced age
- Malnutrition
- Altered renal & liver function
- Effects of underlying disease
- Polypharmacy
- Slowed metabolism
- High body water/ increased volume of distribution
- Decreased protein binding
Pharmacotherapy

- Opiate analgesics
- Sedatives
- Anti psychotics
## Analgesics

<table>
<thead>
<tr>
<th>Drug/Class</th>
<th>Elimination</th>
<th>Onset/Duration</th>
<th>Dosing (IV)</th>
<th>Concentration</th>
<th>Advantages</th>
</tr>
</thead>
<tbody>
<tr>
<td>Morphine sulfate/opioid analgesic</td>
<td>Conjugation; active metabolite excreted renally</td>
<td>5–10 min/2–4 h</td>
<td>LD: 2–4 mg IV push MD: 2–30 mg/h for ventilated patients</td>
<td>100 mg/100 mL NS or D5W</td>
<td>Reduces tachypnea</td>
</tr>
<tr>
<td>Fentanyl/opioid analgesic</td>
<td>Cytochrome P450 3A4 (longer in liver failure)</td>
<td>1–2 min/2–4 h</td>
<td>LD: 25–50 µg IV push MD: 0.7–10 µg/kg/h for ventilated patients</td>
<td>1.25 or 2.5 mg/250 mL NS or D5W</td>
<td>Less hypotension than morphine</td>
</tr>
<tr>
<td>Hydromorphone/opioid analgesic</td>
<td>Hepatic</td>
<td>5 min/2–4 h</td>
<td>LD: 0.2–0.6 mg IV push MD: 0.5–3 mg/h</td>
<td>100 mg/100 mL NS or D5W</td>
<td>May work if patients are tolerant to morphine/fentanyl</td>
</tr>
<tr>
<td>Alfentanil/opioid analgesic</td>
<td>Hepatic; active metabolites excreted renally (dose dependent)</td>
<td>1 min/30–60 min</td>
<td>LD: 50–75 µg/kg slowly over 3 min; MD: 0.5–3 µg/kg/min (usual 1–1.5 µg/kg/min)</td>
<td>10 mg/250 mL NS or D5W</td>
<td>Very short-acting agent</td>
</tr>
<tr>
<td>Remifentanil/opioid analgesic</td>
<td>Titania extansae</td>
<td>1 min/30–60 min</td>
<td>LD: 1 µg/kg over 1 min; MD: 0.6–15 µg/kg/h for MV (unlabeled use); use ideal body weight if &gt; 30% over ideal body weight</td>
<td>5 mg/250 mL NS or D5W</td>
<td>No accumulation in hepatic or renal failure</td>
</tr>
<tr>
<td>Sufentanil/opioid analgesic</td>
<td>Hepatic</td>
<td>1–3 min/30–60 min</td>
<td>LD: 1–2 µg/kg slowly over 3–5 min; MD: 8–50 µg as needed</td>
<td>250 µg/250 mL D5W; variable stability in NS</td>
<td></td>
</tr>
</tbody>
</table>

*(CHEST 2008; 133:552–565)*
# Sedation

<table>
<thead>
<tr>
<th>Drug/Class</th>
<th>Elimination</th>
<th>Onset/Duration</th>
<th>Dosing (IV)</th>
<th>Concentration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lorazepam/</td>
<td>Hepatic conjugation to</td>
<td>5–20 min/6–8 h; up</td>
<td>LD: 2–4 mg IV push MD: 2–6</td>
<td>100 mg/100 mL</td>
</tr>
<tr>
<td>benzodiazepine</td>
<td>inactive metabolite</td>
<td>to 24–72 h in</td>
<td>mg IV q4h-q6h; infusion:</td>
<td>D5W only</td>
</tr>
<tr>
<td></td>
<td>elderly/cirrhosis/</td>
<td>1–10 mg/h; start low in</td>
<td>1–10 mg/h</td>
<td></td>
</tr>
<tr>
<td></td>
<td>ESRD</td>
<td>elderly</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Cytochrome P450 3A4;</td>
<td>5–10 min/1–4 h</td>
<td>LD: 2–5 mg IV push MD: 1–20</td>
<td>100 mg/100 mL</td>
</tr>
<tr>
<td>Midazolam/</td>
<td>active metabolite</td>
<td>(longer in ESRD/</td>
<td>mg/h; start low in elderly</td>
<td>NS or D5W</td>
</tr>
<tr>
<td>benzodiazepine</td>
<td>excreted renally</td>
<td>CHF/liver failure)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Propofol</td>
<td>Conjugation</td>
<td>30–50 s/</td>
<td>MD: 5–150 μg/kg/min</td>
<td>Premixed (10 mg/mL)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>approximately</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>3–10 min (dose</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>dependent)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dexmedetomidine</td>
<td>Hepatic Cytochrome</td>
<td>Immediate/</td>
<td>LD: 0.5–1 μg/kg over 10 min;</td>
<td>100 μg/50 mL</td>
</tr>
<tr>
<td></td>
<td>P450 and</td>
<td>approximately 6</td>
<td>MD: 0.2–0.7 μg/kg/h for 24 h</td>
<td>NS only</td>
</tr>
<tr>
<td></td>
<td>glucuronidation</td>
<td>min (longer in</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Which drug?**

**How to titrate?**

*(CHEST 2008; 133:552–565)*
**Midazolam vs. lorazepam**

- **Midazolam**
  - Faster onset of action- bolus dosing
  - Less duration of action – repeated doing
  - Accumulates in renal / hepatic dysfunction
  - Expensive ( 10 mg ~ Rs 50 )

- **Lorazepam**
  - Long duration of action ( 4-6hrs) – prolonged therapy
  - Cheaper ( 4 mg ~ Rs 15)
  - Carrier toxicity ( propylene glycol – anion gap acidosis )

- **Time to come off sedation**
  - Data conflicting
Propofol

• The active ingredient in Propofol is 2,6-diisopropylphenol in 10% soybean oil, 2.25% glycerol, and 1.2% purified egg phosphatide.

• Disodium EDTA (0.05 mg/ml) or sodium metabisulfite (0.25 mg/ml) is added to inhibit bacterial growth.

• Is hepatically modified & renally excreted

• Key benefits include
  – Rapid onset & offset of action
  – Easy titration
  – Metabolism independent of hepatic & renal function
  – Sedative-hypnotic with anxiolytic & amnestic properties
  – Bronchodialtor, anti-epileptic, muscle relaxant and anti-oxidant
Adverse events

- Hypotension
- Hypertriglyceridemia
- Sepsis due to contamination
- Pancreatitis
- Metabolic acidosis
- Adrenal insufficiency
- Immune dysfunction
- PRIS
- Is very expensive
- Practically no benefit over Midazolam in terms of earlier extubation and shorter stay
Dexmedetomidine

• Is an α2 agonist

• Increasing role, especially in post-operative patients

• Advantages include
  – Maintenance of respiratory drive
  – Rapid awakenings
  – Analgesia
  – Amnesia
  – Good hemodynamic tolerance
  – Decreased requirement for other medications
• Recent meta-analysis of 24 studies
  – Decreased ICU stay
  – Trend towards decreased mortality & delirium
  – Heterogeneity of data
  – Higher incidence of bradycardia

How to give sedation?

- Intermittent boluses preferred
- Consider continuous infusion
  - Requirement more frequent than every 2 hours
  - Unable to achieve target sedation
  - Check for pain / delirium
- If on continuous infusion
  - Titrate dose to target
  - Reassess every few hours
  - Daily interruption of sedation (DIS) & restart at half dose
  - Empiric downward titration after 48 hrs
DIS

• “Wake up & breathe” protocol
  – Earlier extubation
  – Less morbidity
  – Less cost
  – No increase in adverse events (PTSD, recall or cardiac events)

• Should be practiced in all except pts with increased risk for cardiac events
Co-sedation / A1 strategy

Sedation during mechanical ventilation: A trial of benzodiazepine and opiate in combination*

**Objective:** To compare the efficacy of continuous intravenous sedation with midazolam alone vs. midazolam plus fentanyl ("co-sedation") during mechanical ventilation.

**Design:** A randomized, prospective, controlled trial.

**Setting:** A ten-bed medical intensive care unit at a university hospital.

**Patients:** Thirty patients with respiratory failure who were expected to require >48 hrs of mechanical ventilation and who were receiving a sedative regimen that did not include opiate pain control.

**Interventions:** An intravenous infusion of either midazolam alone or co-sedation was administered by a nurse-implemented protocol to achieve a target Ramsay Sedation Score set by the patient's physician. Study duration was 3 days, with a brief daily “wake-up.”

**Measurements and Main Results:** We recorded the number of hours/day that patients were “off-target” with their Ramsay Sedation Scores, the number of dose titrations per day, the incidence of patient-ventilator asynchrony, and the time required to achieve adequate sedation as measures of sedative efficacy. We also recorded sedative cost in U.S. dollars and adverse events including hypotension, hypoventilation, ileus, and coma. Compared with the midazolam-only group, the co-sedation group had fewer hours per day with an “off-target” Ramsay Score (4.2 ± 2.4 and 9.1 ± 4.9, respectively, *p < .002*). Fewer episodes per day of patient-ventilator asynchrony were noted in the co-sedation group compared with midazolam-only (0.4 ± 0.1 and 1.0 ± 0.2, respectively, *p < .05*). Co-sedation also showed nonsignificant trends toward a shorter time to achieve sedation, a need for fewer dose titrations per day, and a lower total sedative drug cost. There was a trend toward more episodes of ileus with co-sedation compared with midazolam-only (2 vs. 0).

**Conclusions:** In mechanically ventilated patients, co-sedation with midazolam and fentanyl by constant infusion provides more reliable sedation and is easier to titrate than midazolam alone, without significant difference in the rate of adverse events. (Crit Care Med 2006; 34:1395–1401)

**Key Words:** sedation; mechanical ventilation; midazolam; fentanyl; benzodiazepine; opiate
Delirium

**Diagnosis**
- DSM IV or CAM-ICU

**Supportive Measures**
- Maintain hydration
- Avoid restraints
- Mobilize patient
- Reduce noise
- Orienting stimuli
- Reassurance
- Bedside sitters, etc.

**Does patient behavior interfere with care or safety?**
- **YES**
  - Low dose neuroleptics and/or short acting BZD
  - Continue evaluation and treatment
- **NO**

**Review History, Medications, Physical Examination, Laboratory, etc.**
- Offending drug? (Discontinue)
- Trauma or focal finding? (CT of brain)
- Focus of infection? (Antibiotics)
- Fever? Meningismus? (Lumbar puncture)
- No obvious cause?
- Patient improves?
- Discharge patient to post ICU setting (NO)

**Consider:**
- B12-folate
- Thyroid testing
- EEG
- Brain MRI
- Drug levels
- Toxicology, etc.

**Reassess patient**
- Consider prolonged delirium
Haloperidol

• Starting doses are 2-10 mg (5 mg) bolus over 5-10 minutes. Repeat every 20 minutes till end-point achieved

• 25% of the cumulative dose q6 hourly for maintenance

• Block 60% of the D2 receptor while avoiding side-effects associated with complete D2 blockade

• Once calm, smaller doses can be used

• Adverse events
  – Extrapyramidal symptoms
  – Malignant hyperthermia
  – Torsade de pointe
Assign sedation goal to optimize comfort and management of critical illness*

Is patient agitated?

- Review causes of agitation (Figure 1); correct reversible causes.

  - Is the patient still agitated?
    - Try non-pharmacologic therapy; optimize environment.
    - Is the patient in pain?
      - Intermittent opiates**
    - Is the patient delirious?**
      - Intermittent neuroleptic agent**
    - Is the patient anxious?
      - Intermittent benzodiazepine or propofol (if short term or need for serial neurologic evaluation)**

- No
  - Review sedation goals daily. Use the lowest dose of medication necessary to ensure comfort. Consider daily interruption if continuous infusion used. Consider empiric taper if prolonged duration of high dose therapy needed.
  - Consider continuous infusion if repeated doses needed.
AGITATION in the ICU

- **PAIN & ANXIETY**
- **VENTILATOR DYSSYNCHRONY**
- **ILLNESS**
- **DELIRIUM**

Specific measures

<table>
<thead>
<tr>
<th>Dangerous agitation</th>
<th>agitation dyssynchrony</th>
<th>Pain anxiety</th>
<th>lightly sedated</th>
<th>deeply sedated</th>
<th>unresponsive</th>
</tr>
</thead>
</table>

Anti-psychotics, Sedatives, analgesics

Dangerous agitation, anxiety, dyssynchrony, lightly sedated, deeply sedated, unresponsive.
• Agitation is a distressing issue in ICU

• “Look around” before reaching for syringe

• Patient focused & target based sedation

• Reassess on a daily basis for pain & delirium

• “Wake up & breathe”