

## Sedation, Analgesia, and Delirium in the Critically Ill Patient:

An Evidence-Based Review Brenton LaRiccia, RPA-C

## Overview

- Analgesia Overview
- Sedation Overview
- Delirium Overview
- Historical perspective
- Current practice
- Future directions

## Analgesia Overview

- Purpose: Treat pain
- Analgesics:
  - Narcotics-
    - Fentanyl
    - Remifentanyl
    - Hydromorphone
    - Morphine
    - Oxycodone, Hydrocodone, etc
  - NSAIDS-
    - Toradol, Ibuprofen, etc

## Analgesia Overview

- Causes of Pain:
  - Surgery, Trauma, existing diseases
  - Catheters, drains
  - Nursing care (i.e. suctioning, PT, dressing changes, mobilization)
- Side effects of untreated pain:
  - Stress response (tachycardia, increased myocardial oxygen consumption, immunosuppression)
  - Agitation, exhaustion, lack of sleep, delirium

## Analgesia Overview

Drug Delivery	Continuous infusions	intermittent IV/PO
Advantages	ease of titration, tighter pain control, steady-state concentration, etc	easy "on/off", easy to treat acute agitation
Disadvantages	Longer duration of activity, greater propensity of delirium, higher overall cost	Potentially time consuming for nursing staff

## Sedation Overview

- Purpose: relieve anxiety, control agitation, facilitate procedures, including mechanical ventilation.
- An ideal regimen should control anxiety and agitation, while minimizing adverse effects.
- Common Drugs:
  - Benzodiazepines
    - Midazolam (Versed)
    - Lorazepam (Ativan)
    - Diazepam (Valium)
  - Propofol
  - Dexmedetomidine (Precedex)

## Sedation Overview

- Adverse effects of excessive sedation include:
  - Ventilator-associated Pneumonia
  - Longer time spent on the ventilator
  - Infections
  - **ICU Delirium**
  - Paradoxical reactions, such as aggression, **agitation**, and **anxiety**
  - Hypotension from decreased systemic vascular resistance (especially in hypovolemic patients)

## Sedation Overview

- Drug Classes of sedative/hypnotics:
  - GABA receptor agonists:
    - Benzodiazepines (midazolam, lorazepam, diazepam, etc)
    - Propofol
  - Alpha 2 agonists:
    - Dexmedetomidine (precedex)

## Sedation Overview

- Dexmedetomidine
  - Provides "...**anxiolysis** via receptors within the locus ceruleus, **analgesia** via receptors in the spinal cord, and attenuation of the stress response with **no significant respiratory depression**."<sup>4</sup>
  - Why not use it on everybody??
    - Exclusion criteria: trauma, burns, severe CNS pathology (i.e. stroke, seizures, dementia), dialysis, LVEF < 30%, >2 vasopressors)
    - bradycardia and hypotension, especially with loading dose (not typically given in ICU)
    - Moral of the story: good for some patients, not for others

## Delirium Overview

DSM-IV requires the following essential criteria for a diagnosis of delirium

**Disturbance of consciousness** (i.e. reduced clarity of awareness of the environment) with reduced ability to focus, sustain, or shift attention.

**Change in cognition** (e.g. memory deficit, disorientation, language disturbance and perceptual disturbance) that is not better accounted for by a pre-existing, established, or evolving dementia.

**Development over a short period of time** (usually hours to days) and disturbance tends to fluctuate during the course of the day.

There is **evidence** from the history, physical examination, or laboratory findings that the disturbance is caused by the direct physiological consequences of a general medical condition.

## Subtypes of Delirium

- *Hyperactive* - paranoid, agitated
  - Readily recognized, best prognosis
  - Purely hyperactive: 1.6% of delirium episodes
- *Hypoactive* - withdrawn, quiet, paranoid
  - "Quiet delirium"
  - Often not well recognized, misdiagnosed
  - Purely hypoactive episodes 43.5%
- *Mixed* - combination
  - Most common in ICU patients 54.9%
  - Worst prognosis

## Causes of Delirium

- The brain generates an inflammatory response in the setting of systemic infections and injury which includes cytokine production, cell infiltration, and tissue damage. This response is thought to alter patterns of neuronal activity, resulting in delirium.
- The three neurotransmitters involved in the pathophysiology of delirium include dopamine,  $\gamma$ -aminobutyric acid (**GABA**), and acetylcholine.

## Everything causes Delirium!

- Precipitating factors include:
  - Hypoxia/metabolic disturbances/electrolyte imbalances
  - withdrawal syndromes
  - acute systemic and intracranial infections
  - seizures, dehydration, hyperthermia
  - head trauma, vascular disorders, immobilization
  - sleep deficiency, psychiatric medications, intracranial space occupying lesions
  - surgery, mechanical ventilation
  - bladder and central venous catheterizations, restraints, and pharmacologic agents, especially benzodiazepines and opioids

## Delirium Screening Tools

- Intensive Care Delirium Screening Checklist (ICDSC)
  - sensitivity of 99%, and specificity of 64%
- Confusion Assessment Method for ICU (CAM-ICU)
  - sensitivity and specificity of approximately 95%
- Others (CTD, NEECHAM, DDS)

## Delirium Treatment

- Pharmacologic
  - Typical antipsychotics – Haldol
  - Atypical antipsychotics – Seroquel, Geodon, Risperdal, Zyprexa
  - Dexmedetomidine?
  - Sleep aids – i.e. Trazodone
- Non-Pharmacologic
  - Restore Sleep/wake cycle (quiet times)
  - Reduce restraint usage
  - Reorient to environment (lights on during day/shades up, lights/TV/Radio off at night, hearing aids, glasses, etc)

## Delirium Tremens

- Pathophysiology: GABA receptor down-regulation
- Diagnostic criteria for Alcohol withdrawal:
  - Cessation/reduction in alcohol use that has been heavy and prolonged
  - Two or more of the following:
    - Autonomic hyperactivity (sweating or HR >100bpm)
    - Increased hand tremor
    - Insomnia
    - Nausea/Vomiting
    - Transient hallucinations/illusions
    - Psychomotor agitation
    - Anxiety
    - Grand mal seizures

## Sedation and Analgesia- Historical Perspective

- No interruptions, minimal weaning
- “keep people snowed”
- Ventilator discomfort

## Historical Perspective

BRITISH MEDICAL JOURNAL 14 APRIL 1979 977

### Continuous narcotic infusions for relief of postoperative pain

JEREMY J CHURCH

British Medical Journal, 1979, 1, 977-979

Summary and conclusions  
Relief of acute pain after surgery or trauma is still inadequate in many centres, most patients being treated with intermittent intramuscular injections of narcotic analgesics. Over the past three years continuous intravenous narcotic infusions have been used at this hospital to treat postoperative pain; recently a system has been devised whereby an hourly dose is given and the dispenser recharged every hour. The method used is cheap and reliable, and signs of over-dosage may be easily checked by nursing staff. Side effects rarely occur. Fifty patients who had received intravenous infusions after undergoing major abdominal surgery were sent a questionnaire to assess postoperative pain, and the results were compared

excessive in the other 20%, and a further adjustment may be necessary within the first four hours. The prescribed infusion rate is then divided on a drip regulator (Dial-a-Flow). Only the hourly dose is added on, the chamber of the microdrip dispenser, which carries a warning notice (Fig 1). Thus the nurse is required to carry out the instructions

THIS PATIENT HAS A PETHIDINE INFUSION

Please ensure that the Metrist is charged every hour with the prescribed hourly dose drip, and count the registration rate. If less than 10 per minute stop the infusion and call the anaesthetist duty registrar.

HOURLY DRIP RATE \_\_\_\_\_ ml

## Sedation and Analgesia- Historical perspective

- The Sedation Interruption, or vacation, was a revolutionary idea when it was proposed.
- NEJM 2000, Kress, et al
  - 128 vented MICU patients
  - Decreased Median vent days from 7.3 to 4.9 days (P=0.004)
  - Decreased ICU length of stay from 9.9 to 6.4 days (P=0.02)
  - Median age for intervention and control groups was 57 and 61, respectively

...So this should work for all ICU patients, Right?

## Are All ICU patients the Same?

- Robinson, et al, Journal of Trauma 2008
- "Analgesia-Sedation-Delirium Protocol"
- 143 patients
- Protocol group had **26.4 ventilator-free days versus control group's 22.8 days**
- **Hospital length of stay was an average of 12 days versus 18 days (P=0.036)**

## Not All ICU patients are the same!

- Different baseline demographics in different ICU's
  - MICU's: Older, less pain needs
  - Surgical/Trauma ICU's: Patient age varies (some older, some younger)
  - More post operative pain
  - Younger patients typically metabolize drugs more rapidly
  - Brain injuries-Different from above patient types

\*Bottom line: Just because they are in the ICU, does NOT mean they can be treated the same!\*

## Current Practice

**CRITICAL CARE SEDATION ORDERS**

This order set is to be used for all intubated patients requiring sedation to facilitate mechanical ventilation. UNIT(S): ICU, CCU, ED

**TARGET RASS SCORE: 0 to 1; 2 or 3: TARGET RASS SCORE**

- Document RASS score every 2 hours and patient response at every assessment point
- Document shift total dose of medications used
- DAILY A.M. Spontaneous Breathing Trial (SBT) (Note: Not for patients on neuromuscular blockade)

**HYPONOTICS:** Preferred agents for sedation of patients **except** those with significant hemodynamic instability.

## Current Practice

Medication	Route	Response	Dose
Propofol	IV	Deep sedation, unresponsive to voice	1-2 mg/kg bolus, then 0.5-1 mg/kg/hr infusion
Midazolam	IV	Deep sedation, unresponsive to voice	0.05-0.1 mg/kg bolus, then 0.05-0.1 mg/kg/hr infusion
Fentanyl	IV	Deep sedation, unresponsive to voice	0.1-0.2 mg bolus, then 0.1-0.2 mg/hr infusion
Hydrocodone	IV	Deep sedation, unresponsive to voice	0.1-0.2 mg bolus, then 0.1-0.2 mg/hr infusion

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## Current Practice

- Sedation Vacation
- Sedation Weaning
- Sedation Protocols
- Daily interruptions
- Hourly neurologic checks with sedation interruptions
- Protocol Overload!

## Two years ago...2009

- Results of a Survey: Delirium and sedation in the intensive care unit: Survey of behaviors and attitudes of 1384 healthcare professionals
- 41 North American hospitals
- 970 physicians, 322 nurses, 23 respiratory therapists, 26 pharmacists, 18 NP/PAs, and 25 others

## Results

- Delirium Results:
  - More than half 59% (774 of 1302) screen for delirium
  - 33% of those respondents (258 of 774) use a delirium screening tool
- Sedation Results:
  - 29% (396 of 1355) of respondents still do not have a sedation protocol
  - A majority (76%, 990 of 1309) have a written policy on spontaneous awakening trials
  - the minority of respondents (44%, 446 of 1019) practice spontaneous awakening trials on more than half of ICU days.

Clearly, there is room for improvement!

## Changing Practice at URMIC

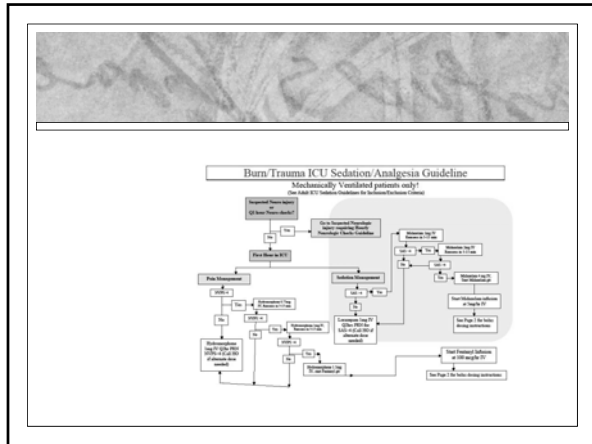
- Sedation Interruption
  - BTICU: 40% compliance in patients not receiving hourly neurologic checks
  - Half of those compliant with sedation interruptions had sedation INCREASED after interruption
- Patients Receiving hourly neurologic checks received more propofol than remifentanyl
  - Partly due to inappropriate use of propofol to treat hypertension not related to agitation

## Patient Specifics

- In the BTICU, there are three general types of patients:
  - Neurosurgery and those needing hourly neurologic checks
  - Young, poly-trauma patients with significant pain and sedation needs
  - Older, general surgery, orthopedics, or other subspecialty that have some pain and sedation needs, but do not need continuous infusions
  - Burns are currently excluded from guideline

## Changing Practice at URMIC

- Guideline-directed sedation by nurses has been shown to decrease the length of mechanical ventilation.
- First phase: aggressive bolus loading patient on arrival to the ICU with pain and sedation medication as needed within first hour, then proceeding to intermittent dosing or continuous infusion.
- Second phase: regimented weaning of both pain and sedation infusions to intermittent dosing, with delirium screening/prevention/treatment



**AFTER 1<sup>ST</sup> DOSE OF SEDATIVE, IF THE PATIENT IS PLACED ON CONTINUOUS SEDATION:**

**FOR BURN TRAUMA ICU PATIENTS AND/OR AGITATED**

Proposed Sedation: 0.5 mg/kg IV of 0.5% propofol or 0.5 mg/kg IV of 0.5% propofol or 0.5 mg/kg IV of 0.5% propofol  
 Titration Sedation: 0.5 mg/kg IV of 0.5% propofol or 0.5 mg/kg IV of 0.5% propofol or 0.5 mg/kg IV of 0.5% propofol

**IF PATIENT IS ON CONTINUOUS SEDATION:**

IF patient has **Respiratory Acidosis**, consider sedation and analgesia modifications to facilitate weaning from Mechanical Ventilation (MV) if patient does not achieve above weaning parameters. OR, if patient is placed on the CPAP or BIPAP, proceed.

**IF THE PATIENT IS ON CONTINUOUS SEDATION AND/OR AGITATED:**

IF patient has **Respiratory Acidosis**, consider sedation and analgesia modifications to facilitate weaning from Mechanical Ventilation (MV) if patient does not achieve above weaning parameters. OR, if patient is placed on the CPAP or BIPAP, proceed.

**Suspected Neurologic injury requiring Emergent Neurologic Consult**  
 One Adult ICU Inpatient to Sedation/Analgesia Clinical

**ANALGESIA:**

IF patient has **Respiratory Acidosis**, consider sedation and analgesia modifications to facilitate weaning from Mechanical Ventilation (MV) if patient does not achieve above weaning parameters. OR, if patient is placed on the CPAP or BIPAP, proceed.

**SEDATION:**

IF patient has **Respiratory Acidosis**, consider sedation and analgesia modifications to facilitate weaning from Mechanical Ventilation (MV) if patient does not achieve above weaning parameters. OR, if patient is placed on the CPAP or BIPAP, proceed.

## Trial Period: January-March 2011

- Total Vented Patients: N=63
- Excluded: N = 5 ( Burn ) ( 9% )
- Eligible for Guideline: N = 58
- Placed on Guideline: N = 52 ( 90% )
- 90% Compliance Achieved for placing patients on Sedation/Analgesia Guideline

### Total 1<sup>st</sup> Quarter BTICU Admissions, by number and percentage

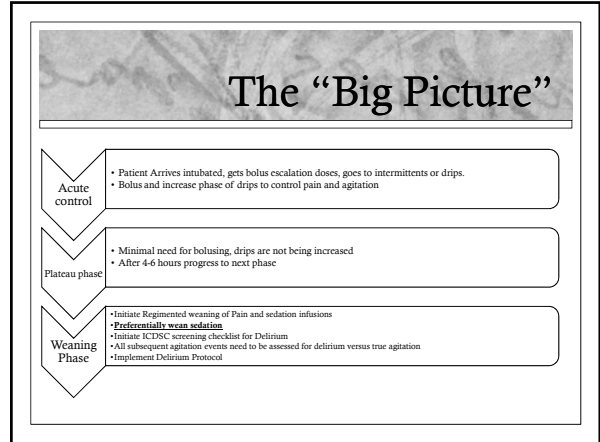
	2011%	2010%	2011#	2010#
Neurosurgery	40%	35%	66	57
Plastics	7%	6%	12	9
Orthopedics	5%	9%	8	15
Trauma	29%	34%	48	54
Acute Care Surgery	16%	12%	27	20

### Reductions in average vent days per patient, as well as average adjusted sedation days in 2011 compared to 2010

	January – March (1 <sup>st</sup> Quarter) 2011	January – March (1 <sup>st</sup> Quarter) 2010
Total Patient Census	164 patients	161 patients
Average Vent Days per patient	5.58 days	6.65 days
Average adjusted sedation days	61.74 days/month	135.78 days/month

## Total Ventilator Days

Ventilator Days (adjusted)	2011	2010	% Decrease from '10 to '11
January	160	179	11%
February	119	174	32%
March	227	190	-19%



- ## Implementation and Compliance
- Multidisciplinary
    - Nursing education
      - Online Learning
      - Nursing Sedation Committee
      - 24/7 ICU presence of Nursing "Sedation Champions"
    - Clinical Pharmacist Support
    - Attending Support/PA/NP involvement
      - Resident Orientation (including copy of guideline)

## Future Directions?

**A protocol of no sedation for critically ill patients receiving mechanical ventilation: a randomised trial**

Thomas Strom, Torben Martinussen, Palle Tjøll

**Summary**  
 Background: Standard treatment of critically ill patients undergoing mechanical ventilation is continuous sedation. Daily interruption of sedation has a beneficial effect, and in the general intensive care unit of Odense University Hospital, Denmark, standard practice is a protocol of no sedation. We aimed to establish whether duration of mechanical ventilation could be reduced with a protocol of no sedation versus daily interruption of sedation.

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