SEDATION / ANALGESIA for Brain Failure Patient

INASNACC
Neuroendocrinological metabolic responses to surgical or traumatic injury

- Endocrine: increase in ACTH, cortisol, ADH, GH, glucagon, renin, aldosterone, decrease in insulin
- Metabolic:
  - CH: hyperglycemia, insulin resistance, glucose intolerance
  - Protein: increase catabolism
  - Fat: increase lipolysis
- Water and electrolyte: Retention of water and sodium, K+ excretion increase

Park GR et al. Sedation and analgesia in the Critically ill. 1995
Factors implicated in the activation of the stress response

- Anxiety, fear
- Pain
- Hypothermia, hyperthermia
- Hypovolemia
- Acidosis
- Starvation, dehydration
- Hypoxia, infection/sepsis
- Prolonged immobilization

Park GR et al. Sedation and analgesia in the Critically ill. 1995
Factors Provoking Anxiety

- Inconsiderate Providers
- Chemical/Physiologic Imbalance
- Medications
- Alarms
- Mechanical Devices
- Nonchanging Environment
- Memory Loss
- Confusion
- Fear
- Sleep Deprivation
- Loss of Control
- Surgical Stress
- Temperature
- Noises
- Lights
- ICU Psychosis

Articles on Sedation
Sedation

- Components?
  - Hypnosis
  - Anxiolysis
  - Amnesia
  - Analgesia
Sedation/analgesia

- A state with allows patients to tolerate unpleasant procedures while maintaining adequate cardiorespiratory function and the ability to respond purposefully to verbal command or tactile stimulation.

ASA
Sedation/analgesia

- Verbal communication possible
- Airway reflexes intact
- Airway dilator muscle functional
- Respiratory control intact
- Airway intervention unlikely
- Unplanned intubation unlikely
- Respiratory complication unlikely
Deep sedation or GA with an unprotected airway

- Verbal communication impossible
- Airway reflexes attenuated
- Airway dilator muscle dysfunctional
- Respiratory control impaired
- Airway intervention likely
- Unplanned intubation likely
- Respiratory complication likely
Goals of sedation and analgesia

- Patient comfort, Control of pain
- Anxiolysis and amnesia
- Blunting autonomic responses
- Facilitate nursing and management
- Patient protection - avoid self-extubation
- Reduced oxygen consumption
- Ventilator synchrony
- Avoidance of muscle relaxants
- Avoidance of post-traumatic stress
- Normal sleep pattern
Sedation for patient comfort

- Under sedation with associated agitation affects 57% - 71% adult ICU patients.
- Severe agitation affects 43% of ICU patients.
- Only 50% were amnesic for their ICU stay.
  
  Sessler CN et al. Chest. 1992
  Fraser GL et al. Pharmacotherapy. 2000

- ICU patients commonly remove medical devices, such as ETT or vascular catheters and these events are often associated with agitation.
  
  Fraser et al. Int Pharmac Abstr. 1999
### The spectrum of sedation

<table>
<thead>
<tr>
<th>Undersedation</th>
<th>Oversedation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Agitation</td>
<td>Prolonged sedation</td>
</tr>
<tr>
<td>Increase oxygen consumption</td>
<td>Respiratory depression</td>
</tr>
<tr>
<td>Pain and discomfort</td>
<td>Hypotension</td>
</tr>
<tr>
<td>Catheter displacement</td>
<td>Bradycardia</td>
</tr>
<tr>
<td>Inadequate ventilation</td>
<td>Ileus</td>
</tr>
<tr>
<td>Hypertension</td>
<td>Increase protein breakdown</td>
</tr>
<tr>
<td>Tachycardia</td>
<td>Immunosuppression</td>
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<tr>
<td>Hypoxia</td>
<td>Renal dysfunction</td>
</tr>
<tr>
<td>Accidental extubation</td>
<td>Deep venous thrombosis</td>
</tr>
<tr>
<td>Patient injury</td>
<td>Hepatotoxicity</td>
</tr>
</tbody>
</table>
Effort to avoid problems associated with undersedation

- Oversedation → that lead to prolonged ventilatory support, longer ICU stay, medical evaluation for failure to awaken, increase risk of infection, high cost.

Riker RR, WCA 2000, Canada
Over-sedation

- Respiratory depression
- Hypotension
- Bradycardia
- Immunosuppression
- Venous stasis
- Increased time on ventilator
- Increased time in ICU
- Increased cost
- Failure to recognize cerebral insult
- May cause cognitive dysfunction
Respiratory depression

- The only parameters that correlate with respiratory depression in extubated patients are:
  - level of sedation
  - respiratory pattern

- Respiratory rate and end-tidal CO$_2$ measured via nasal cannula do not correlate

Pitfall of pulse oximetry

- The pulse oximeter is a LATE detector of respiratory depression if supplemental oxygen is being administered.
Sedation scales

- Avoid over-sedation and under-sedation
- Define an optimal endpoint for titration of sedation
- Provide continuity of care and charting
- Facilitate cost-effective use of drugs
- Allow comparison of drugs
- Enable precise patient management
Current sedation scales

- Ramsay Scale
- Sedation–Agitation Scale (SAS)
- Bispectral index (BIS) monitoring
- Brussels Sedation Scale
- Over 30 scales available
Ramsay Sedation Scale

Level of sedation:

1  Patient is anxious and agitated or restless, or both
2  Patient is cooperative, oriented and tranquil
3  Patient responds to commands only
4  Patient exhibits brisk response to light glabellar tap or loud auditory stimulus
5  Patient exhibits a sluggish response to light glabellar tap or loud auditory stimulus
6  Patient exhibits no response
Sedation–Agitation Scale (SAS)

7 Dangerous agitation
6 Very agitated
5 Agitated
4 Calm and cooperative
3 Sedated
2 Very sedated
1 Unrousable

Brussels Sedation Scale

1  Unrousable
2  Responds to pain stimulus
3  Responds to auditory stimulus
4  Awake and calm
5  Agitated

Ideal sedative

- Rapid onset and recovery
- Lack of accumulation
- Easy titration to desired level
- Haemodynamic stability
- Lack of respiratory depression
- Absence of tolerance or withdrawal
- Improved ease of patient management
- Facilitates patient communication
- Cost-effective
Choice of agent: the ideal sedative agent

- Decrease CMRO2 while preserving oxygen supply to the brain.
- Lower ICP without decreasing CPP.
- Maintain cerebral autoregulation and vascular reactivity to CO2.
- Fast and smooth onset of action.
- Easily controllable maintenance of depth and duration of sedation.
- Enable therapeutic windows for the evaluation of neurological status and complications.
Intensive Care Sedation & Analgesia--Need for a New Approach?

Problems with Current Methods

• Respiratory depression
• Gastrointestinal effects (e.g. constipation)
• Hemodynamic effects (e.g. low BP, cardiac output)
• Tolerance
• Withdrawal leads to agitation
## Problem with current sedative agent

*Duke et al. ICCS, 1998*

<table>
<thead>
<tr>
<th></th>
<th>Midazolam</th>
<th>Propofol</th>
<th>Opioids</th>
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<tbody>
<tr>
<td>Prolonged weaning</td>
<td>X</td>
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<td>X</td>
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<tr>
<td>Respiratory depression</td>
<td>X</td>
<td>-</td>
<td>X</td>
</tr>
<tr>
<td>Severe hypotension</td>
<td>X</td>
<td>X</td>
<td>-</td>
</tr>
<tr>
<td>Tolerance</td>
<td>X</td>
<td>-</td>
<td>X</td>
</tr>
<tr>
<td>Hyperlipidaemia</td>
<td>-</td>
<td>X</td>
<td>-</td>
</tr>
<tr>
<td>Increase infection</td>
<td>-</td>
<td>X</td>
<td>-</td>
</tr>
<tr>
<td>Constipation</td>
<td>-</td>
<td>-</td>
<td>X</td>
</tr>
<tr>
<td>Lack of orientation and cooperation</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Abuse potential</td>
<td>x</td>
<td>X</td>
<td>x</td>
</tr>
</tbody>
</table>
When to use which drug?

-2-

Long Term

Comparisons of midazolam and lorazepam show comparable or even shorter awakening with lorazepam


Midazolam

- Rapid onset
- Cardiostable
- $T_{1/2}$ Healthy Volunteers - 1.5 - 3 hours
- $T_{1/2}$ ICU - 8.9 hours - huge interpatient variability
- $\alpha$-hydroxymidazolam - 10% activity
- Glucuronidated $\alpha$-hydroxymidazolam
- Cytochrome $P_{450}$ 3A4 - drug interaction
Lorazepam

- Slow onset
- Cardiostable
- $T_{1/2} \beta$ Healthy Volunteers - 10-20 hours
- $T_{1/2} \beta$ ICU - 13.8 hours
- But interpatient variability does not exist to extent with midazolam
- Metabolism independent liver function or co-medication
How to use each drug?

- Sedation Scores
- Agreed Level of Sedation

- Sedation Protocols
  - The use of protocols can reduce the duration of mechanical ventilation, ICU and Hospital stay, and the need for tracheostomy.

  Crit Care Med 1999. 27(12); 2609.
How to use each drug?

-2-

- Intermittent verses Continuous sedation
  - Use of continuous IV sedation may be associated with the prolongation of mechanical ventilation
    Chest 1998. 114(2); 541.

- Daily interruption of Sedation
  - Reduces duration of mechanical ventilation and length of ICU stay
    NEJM 2000. 342(20); 1471.
Drug infusions stopped until patient awake or agitated

Effect on patient comfort and recall

Confirms other studies that suggest excessive use of sedatives result in prolonged mechanical ventilation and ICU stay

- Kollef MH et al. The use of continuous i.V. Sedation is associated with prolongation of mechanical ventilation. Chest 1998;114:541-8

Problems with this study …..
Sedation in the ICU

In patients receiving mechanical ventilation, daily interruption of sedative-drug infusions decreased duration of mechanical ventilation and length of ICU stay

$\alpha_2$-Adrenergic Agents

- CBF .................................. Reduced
- $\text{CMRO}_2$ ........................ Unchanged
- Uncoupling ....................... No Ischemia
- Cerebrovascular Reactivity ........ Maintained (by up to 50%)
- Autoregulation ................. Maintained (60 – 180)
- Cerebral Vasoconstriction .......... Arterial & Capacitance
- Cerebral Blood Volume .......... Reduced
What about Neuro patients

Types of patients in Neuro ICU

Post operative routine

Complicated post operative

Trauma

Acute brain syndrome
Brain Injuries

- Spontaneous hyperventilation continues
- Pain control significant
- Adjustment to arousable patient
- Involve other paramedical personnel
- Additional opioids & sedation
  - Necessary in some
  - Reduced dosage
Longer Term Use of Dexmedetomidine

- “Myocardial protective”
- Lower heart rate
- ? Less cardiac arrhythmias
- ? No accumulation
- ? Immune suppressive effect of alpha 2 agonists
- Increased awareness on ICU
- ? Lacks amnesic properties
Precedex has a place in short and long term sedation

Patient selection is vital

Accept failures

Unknowns
Thank you very much