SEDATION / ANALGESIA for Brain Failure Patient

INASNACC

Neuroendocrinological metabolic responses to surgical or traumatic injury

- Endocrine : increase in ACTH, cortisol, ADH, GH, glucagon, renin, aldosteron, 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

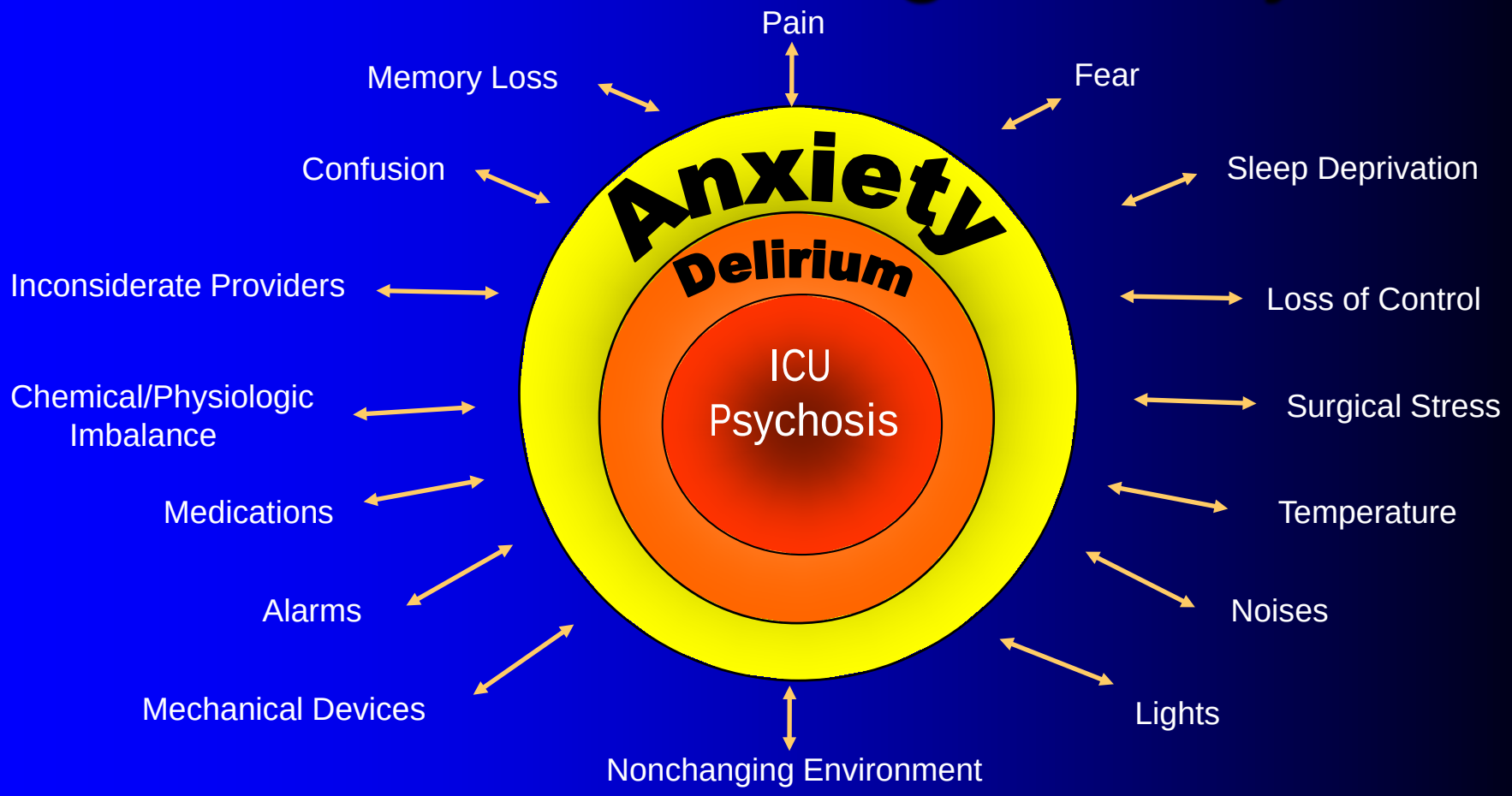
Park GR et al. Sedation and analgesia in the Critically ill.1995

Factors implicated in the activation of the stress response

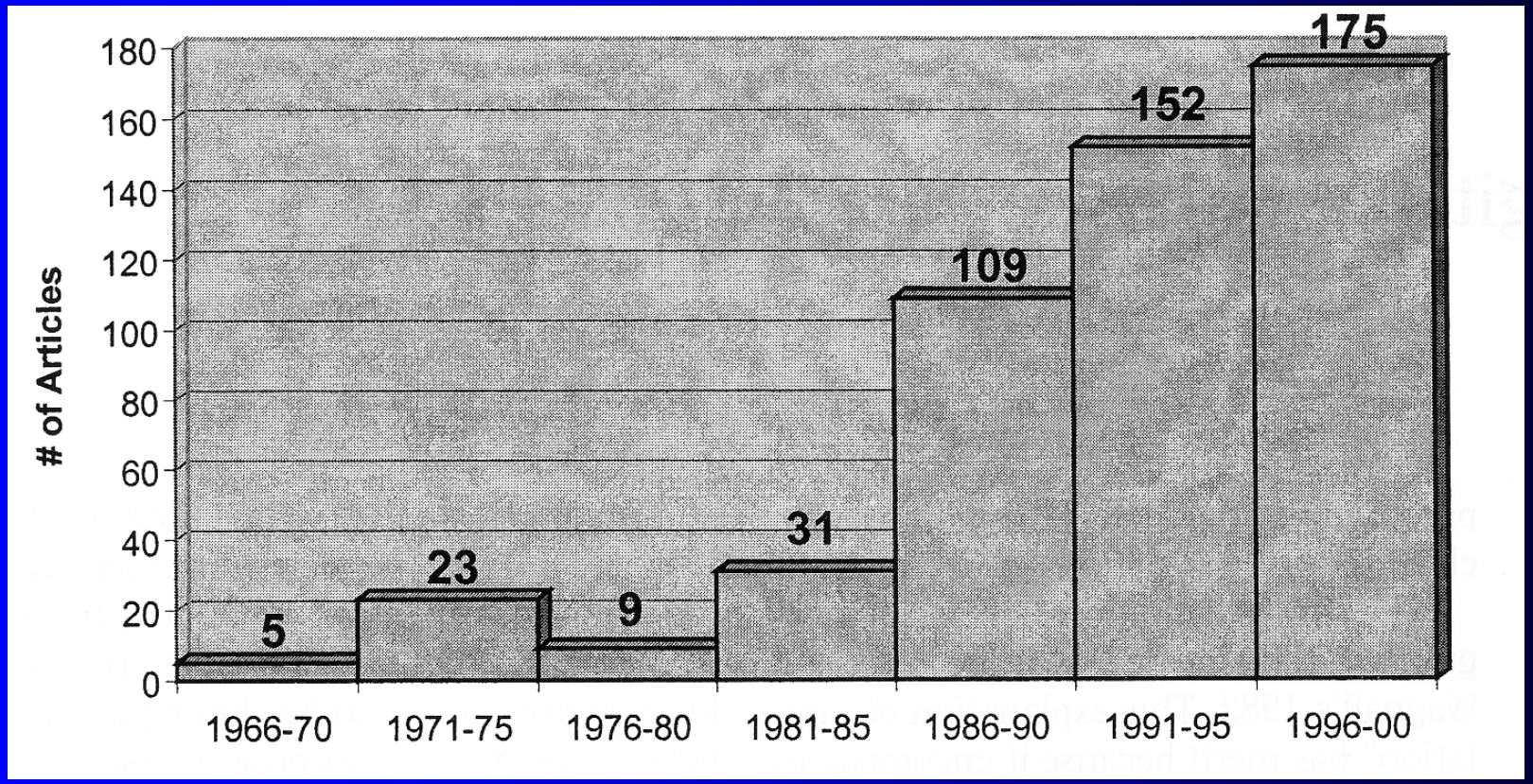
- Anxiety, fear
- Pain
- Hypothermia, hyperthermia
- Hypovolemia
- Acidosis
- Starvation, dehydration
- Hypoxia, infection/sepsis
- Prolonged immobilization

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

Factors Provoking Anxiety



Tesar, Stern. *J Intensive Care Med*. 1986;1:137-148. Harvey. *Am J Crit Care*. 1996;5:7-16. Crippen. *Crit Care Clin*. 1990;6:369-392.



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 purpose fully 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 event are often associated with agitation

Fraser et al. Int Pharmac Abstr. 1999

The spectrum of sedation

Undersedation	Oversedation
Agitation	Prolonged sedation
Increase oxygen consumption	Respiratory depression
Pain and discomfort	Hypotension
Catheter displacement	Bradycardia
Inadequate ventilation	Ileus
Hypertension	Increase protein breakdown
Tachycardia	Immunosuppression
Hypoxia	Renal dysfunction
Accidental extubation	Deep venous thrombosis
Patient injury	Hepatotoxicity

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

Rudolph *et al. Anesth Analg* 1998; 86: S227.

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

Riker *et al*. *Crit Care Med* 1994; 22: 433–40.

Brussels Sedation Scale

1 Unrousable

2 Responds to pain stimulus

3 Responds to auditory stimulus

4 Awake and calm

5 Agitated

Detriche *et al. Br J Anaesth* 1999; 83: 698–701.

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 theurapeutic 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

	Midazolam	Propofol	Opioids
Prolonged weaning	X	-	X
Respiratory depression	X	-	X
Severe hypotension	X	X	-
Tolerance	X	-	X
Hyperlipidaemia	-	X	-
Increase infection	-	X	-
Constipation	-	-	X
Lack of orientation and cooperation	X	X	X
Abuse potential	x	X	x

When to use which drug?

-2-

- Long Term

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

  Krosner *et al*. 1994, Crit Care Med; 22: A54

  Pohlman *et al*. 1994, Crit Care Med; 22: 1241-1247.

Midazolam

- Rapid onset
- Cardiostable
- $T_{½}ß$ Healthy Volunteers - 1.5 - 3 hours
- $T_{½}ß$ ICU - 8.9 hours - huge interpatient variability
- α-hydroxymidazolam - 10% activity
- Glucuronidated α-hydroxymidazolam
- Cytochrome P_{450} 3A4 - drug interaction

Lorazepam

- Slow onset
- Cardiostable
- $T_{½}$ß Healthy Volunteers - 10-20 hours
- $T_{½}$ß 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?

-1-

- 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
  - *Kress JP et al.Daily interruption of sedative infusions in critically ill patients undergoing mechanical ventilation. N Engl J med 2000;342:1471-7*

α_2-Adrenergic Agents

- CBF …… Reduced
- $CMRO_2$ …….. 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

Dexmeditomidine & Neurologic Injury

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

Conclusion

- Precedex has a place in short and long term sedation
- Patient selaction is vital
- Accept failures
- Unkowns

Thank you very much