SEDATING THE NEURO CRITICAL CARE PATIENT

CURRENT AND EVOLVING TRENDS

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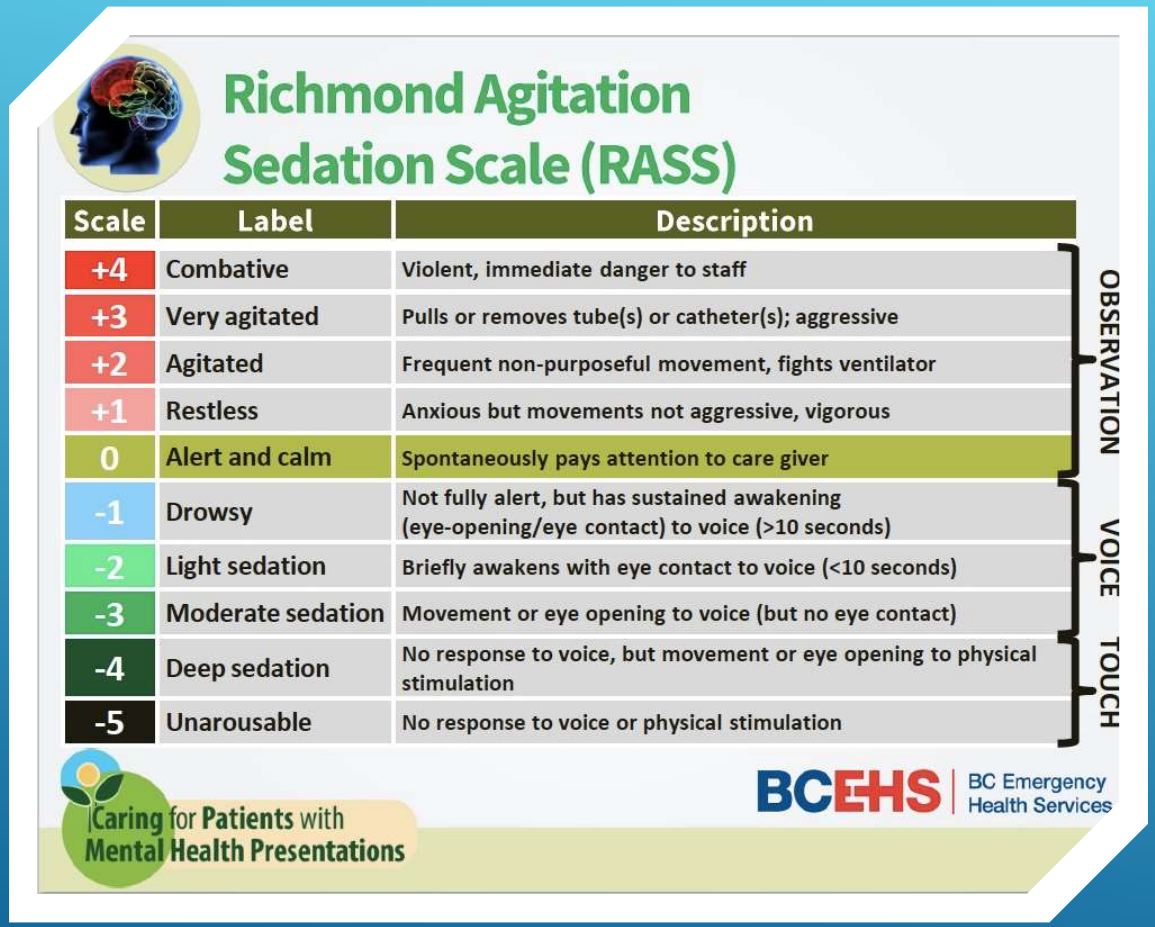
Indications for sedating the Neuro ICU patient

- Ventilator Dependent Respiratory Failure related to:
  Acute Brain Injury, Traumatic Brain Injury, Coma,
  Status Epilepticus, Stroke, Intracranial Hemorrhage
- Ventilator Desynchrony
- Airway protection: loss of protective reflexes
- Decrease CMRO2
- Increased ICP, Placement of External ventricular drainage catheter
- Delerium/Agitation
- Cardiac Arrest



Richmond Agitation Sedation Scale (RASS)

Scale	Label	Description	
+4	Combative	Violent, immediate danger to staff	OBSERVATION
+3	Very agitated	Pulls or removes tube(s) or catheter(s); aggressive	
+2	Agitated	Frequent non-purposeful movement, fights ventilator	
+1	Restless	Anxious but movements not aggressive, vigorous	
0	Alert and calm	Spontaneously pays attention to care giver	
-1	Drowsy	Not fully alert, but has sustained awakening (eye-opening/eye contact) to voice (>10 seconds)	VOICE
-2	Light sedation	Briefly awakens with eye contact to voice (<10 seconds)	
-3	Moderate sedation	Movement or eye opening to voice (but no eye contact)	
-4	Deep sedation	No response to voice, but movement or eye opening to physical stimulation	TOUCH
-5	Unarousable	No response to voice or physical stimulation	

Caring for Patients with Mental Health Presentations

BCEHS | BC Emergency Health Services

LEVELS OF SEDATION

IDEAL SEDATING AGENT FOR THE NEURO PATIENT

- Readily available and inexpensive
- Anti-convulsant
- Maintains Cerebral Perfusion Pressure
- Reduces ICP
- Anxiolytic
- Analgesic
- Preserves spontaneous respiration
- Ability to produce burst suppression
- Rapid onset and non organ dependent metabolism
- Easy Titratability and reversibility
- Limit ICU stays

NO Single Agent satisfies all the goals of sedating the Neuro ICU Patient

COMMON AGENTS UTILIZED FOR SEDATION IN THE ICU

- Propofol
- Benzodiazepines
- Dexmedetomidine
- Opioids
- Volatile Agents (not currently approved in the US)

PROPOFOL

- Sedative Hypnotic
- Not belonging to a specific class of drug
- Utilized for sedation and general anesthesia
- Pharmokinetics: interaction with the neurotransmitter GABA: the principle inhibitory neurotransmitter in the brain
- Metabolism: Hepatic with renal excretion

ADVANTAGES OF PROPOFOL

- Rapid onset
- Easily titratable: Sedation dosing: 5 to 100 mcg/kg/min
- Rapid awakening
- Minimal residual hangover effects
- Decreases ICP
- Decreases Cerebral metabolic rate for Oxygen (CMRo2)
- Can produce Burst Suppression
- Provides antiemetic and antinausea properties

DISADVANTAGES OF PROPOFOL

- Pain on injection
- Potential Allergy related to the structure of the drug, solvent or the preservative
- Does not provide analgesia or anxiolysis
- Dose dependant depression of ventilation
- Decreases SBP, SVR and CBF
- Propofol Infusion Syndrome
- Not Reversible

PROPOFOL INFUSION SYNDROME

- Lethal condition characterized by multiple organ system failure
- Related to prolonged administration of propofol in mechanically ventilated patients
- Presenting features: cardiovascular dysfunction, impairment of cardiovascular contractility, metabolic and lactic acidosis, rhabdomyolysis, hyperkalemia, lipidaemia, hepatomegaly, acute renal failure and eventual mortality
- Risk factors: increased serum catecholamines, steroid therapy, obesity, young age (below 3 years), depleted carbohydrate stores, increased serum lipids (TPN) and extended dosages of Propofol
- Must monitor the patient's ECG, serum creatine kinase, lipase, amylase, lactate, liver enzymes and urine myoglobinurinia with prolonged propofol sedation

TREATMENT OF PROPOFOL INFUSION SYNDROME

- Discontinue Propofol infusion
- Treat metabolic and lactic acidosis with Sodium Bicarb, hemodialysis, hemofiltration
- Manage cardiovascular effects with cardiac pacing, inotropes and vasopressors
- ECMO: extracorporeal membrane oxygenation
- Manage hyperkalemia with calcium, insulin and beta-2 agonists

DEXMEDETOMIDINE

- Pharmacokinetics: Highly selective Alpha-2 Adrenoreceptor agonist
- Provides sedation and anxiolysis via receptors in the locus coeruleus in the pons of the brainstem (involved with the stress and pain response)
- Provides analgesia via receptors in the spinal cord
- Attenuates the stress response with no significant respiratory depression

ADVANTAGES OF DEXMEDETOMIDINE

- Decreases opioid requirements
- Less Respiratory depression, Can be continued after a patient is extubated
- Titratable Dosing .1 to .5 mcg/kg/hr infusion
- Short acting: 60 to 120 minutes, dose dependent
- Prevention and reduction in delirium in the ICU patient
- The calm and cooperative patient, the choice for the nonintubated patient

DISADVANTAGES OF DEXMEDETOMIDINE

- **Hypertension related to Alpha 2 vasoconstriction**
- **Hypotension: especially in the hypovolemic patient**
- **Bradycardia related to depression of the SA and AV nodes and sympatholytic effects**
- **Bolus may lead to Increase BP with a reflex drop in HR**
- **No reversal agent**

- Antagonism of specific receptors in the central nervous system: mu, delta and kappa receptors
- Mu1 receptor provides analgesia, euphoria , miosis
- Mu2 is responsible of hypoventilation, bradycardia, constipation and physical dependence
- Disadvantages : pruritus, nausea and vomiting, urinary retention and depression of ventilation

OPIOIDS

MOST COMMONLY UTILIZED OPIOIDS

- Morphine and Dilaudid
- Fentanyl
- Remifentanil

FENTANYL

- 75 to 125 times more potent than morphine
- Dosing .5 to 1 ug/kg/hr
- Rapid onset
- Hemodynamic stability
- Short duration of action
- Titratable and reversible
- Minimal effects on CBF and CMRO2
- Metabolized in the liver
- Patient and family concerns

REMIFENTANIL

- Ultrashort acting fentanyl derivative
- Rapid onset approximately 1 minute
- Metabolized by plasma esterases, non organ dependent metabolism
- Offset time 3 to 10 minutes
- Decreased ventilator weaning times compared to other opioids
- Titratable and reversible
- Utilized significantly in neuroanesthesia with intraoperative neuromonitoring
- Conscious sedation doses .01 to .02 ug/kg/min
- Downfall: Cost, needs to be reconstituted

BENZODIAZEPINES

- Pharmakokinetics: enhance the effect of the neurotransmitter GABA (gamma-aminobutyric acid) at the GABA receptor, resulting in a sedative with hypnotic, anxiolytic, anticonvulsant, and muscle relaxant properties
- **Midazolam** is the most common benzodiazepine utilized for sedation
- Rapid onset: 3 to five minutes and 1 to 2.5 hour duration of action
- Eliminated through the kidneys
- Titratable and reversible (Flumazenil)

REMIMAZOLAM

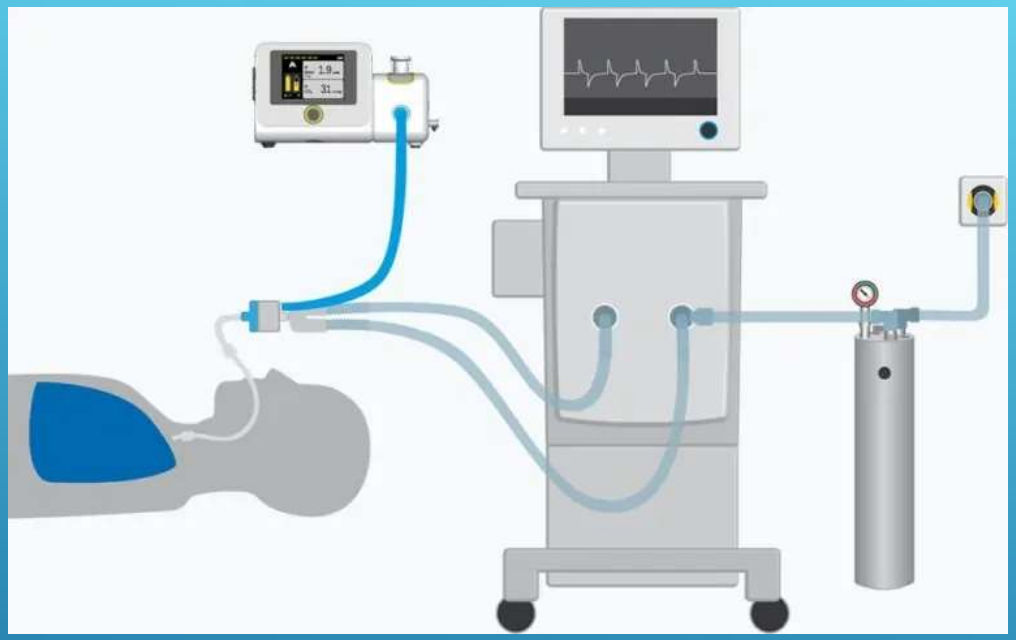
- Ultrashort-acting IV benzodiazepine: combination of midazolam and remifentanil
- More rapid onset and recovery than Midazolam
- Organ independent metabolism: hydrolyzed by tissue esterases enzymes in the blood to an inactive metabolite and excreted in the urine
- Titratable and reversible (Flumazenil)
- No significant effects on HR, ECG ,BP and Respiratory rate
- Currently only approved for procedural sedation
- Disadvantage: COST and must be reconstituted from a powder for IV use

INHALATION AGENTS

Isoflurane and Sevoflurane

VOLATILE AGENTS

- Most Commonly used: Isoflurane and Sevoflurane
- Reduce presynaptic excitation and neurotransmitter release through inhibition of Sodium and Calcium gated channels
- Reduce neurotransmitter activity on both pre and post synaptic nerve membranes via complex interactions with multiple proteins
- Not currently approved in the United States but used in Europe and Canada, Asia and Africa



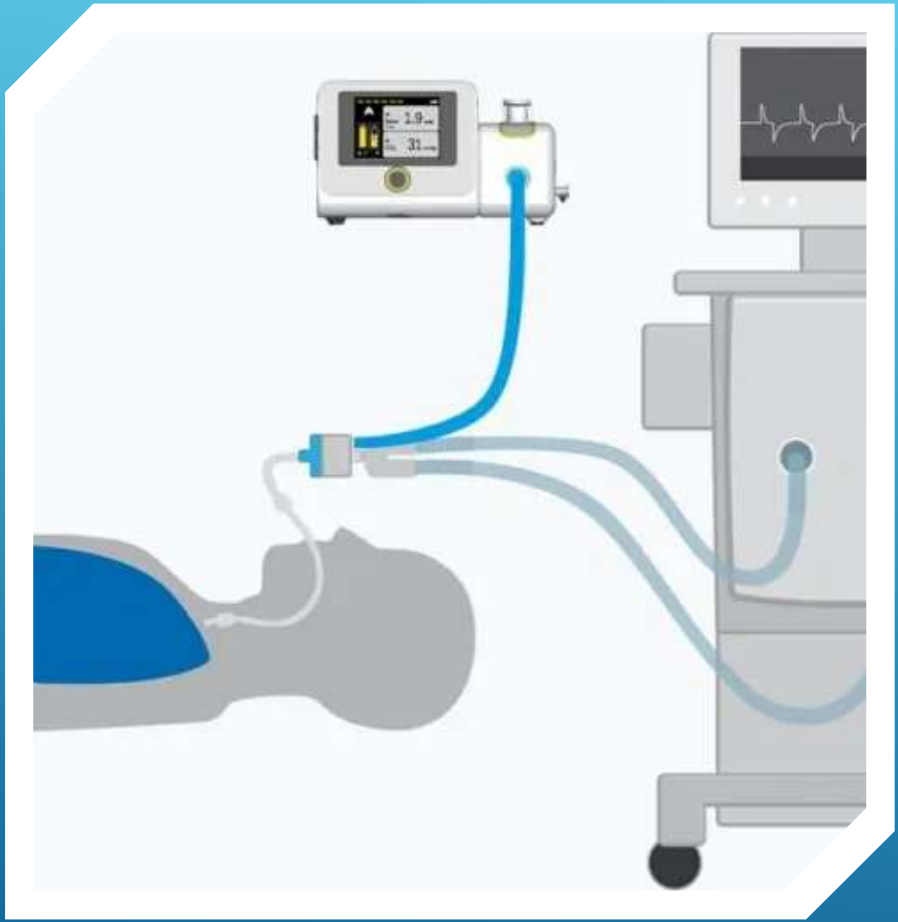
VOLATILE ANESTHETICS

ADVANTAGES TO VOLATILE ANESTHETICS

- Rapid onset and offset of action
- Provides hypnosis, amnesia and analgesia
- Used in cases of intractable status epilepticus
- Preserve cerebral vascular response to changes in Paco2
- Readily availability
- No significant tolerance or withdrawal
- Real time monitoring of inhaled and exhaled concentrations
- Drug clearance via pulmonary exhalation
- Low levels of hepatic metabolism and no active metabolites
- Bronchodilators
- Anticonvulsant effect
- Titratable

DISADVANTAGES OF VOLATILE AGENTS

- Dose dependent cerebral vasodilation, potential rise in ICP
- Dose dependent hypotension
- Risk of Malignant Hyperthermia: a disorder of the skeletal muscle leading to a hypermetabolic response in response to a triggering agent like volatile agent or succinylcholine
- Need for an MH cart with Dantrolene
- Potential rise in fluoride levels (Sevoflurane)
- Requires specialized equipment
- More labor intensive: Nursing, Respiratory and Pharmacy



- Currently two available delivery systems: AnaConDa (Sedana Medical, Sweden) and Mirus System (Pall Medical, Germany)
- Allow the ability to titrate concentration of gas to desired end tidal concentration, integrated gas analysis, and the ability to monitor respiratory parameters (tidal volume, gas flow, ventilatory pressures, PEEP

VOLATILE ANESTHETIC DELIVERY SYSTEMS

ANESTHESIA DELIVERY SYSTEM ADVANTAGES

- Ease of titration to specific concentration (typically one third MAC)
- Real time bedside breath by breath monitoring of inspired and expired gas concentrations
- End tidal gas concentration provides good correlation of cerebral concentration
- Reduced recovery and emergence times
- Quicker extubation times
- +/_ Cost compared to IV sedation

VOLATILE ANESTHESIA DELIVERY SYSTEM DISADVANTAGES

- Require specialized anesthesia volatile agent delivery system
- Gas scavenging and end tidal gas monitoring is required
- Require a minimum tidal volume of 300 to 350 ml
- Drug delivery may be impeded by patient with high volume bronchial secretions
- Increases the dead space in the ventilator circuit by approximately 100 ml

DAILY SEDATION HOLIDAY

DETERMINE IF SEDATION IS STILL REQUIRED

OPPORTUNITY TO ASSESS AND TITRATE SEDATION

CHOOSING THE APPROPRIATE SEDATION REGIMEN

CONSEQUENCES OF OVERSEDATION

- Increased morbidity
- Prolonged ventilation and associated pneumonia
- Muscle atrophy
- Venous stasis and thrombosis
- Increased ICU stays/cost
- A trip to CT Scan

CONSEQUENCES OF UNDERSEDATION

- Anxiety and agitation
- Pain
- Increased ICP/CMRO2
- Tachycardia
- Hypertension
- Ineffective ventilation and ventilatory dysynchrony
- Wound disruption
- Accidental removal of tubes, catheters, and lines
- Fall risk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THANK YOU AND QUESTIONS