A Bad Night in the PICU

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Speaker introduction

- Dr. Marisa Mize has dedicated her career to the bedside of the critically ill child. She currently works as a PNP in pediatric intensive care. In addition to her clinical practice, she is continually involved with the education of the pediatric critical care practitioners and nurses. She is currently adjunct professor of nursing at Catholic University of America, teaching courses on both graduate and undergraduate levels. She precepts PNP students in the intensive care unit. She has developed a course for PNP students that cover the care, management, and treatment of the acute and critically ill child. This course is taught annually and is a requirement for PNP students who are going to pursue the acute care certification. She lectures both nationally and internationally on pediatric critical care issues. She has co-chaired a national conference for care of the critically ill child for the past several years, working with nurses, nurse practitioners and physicians to bring about a conference that addresses current issues in the care of the critically ill child.

Conflict

- None

Objectives

- Review three types of pediatric critical care challenges:
  - Respiratory distress/failure
  - Traumatic brain injury
  - Sedation for mechanically ventilated children
- Utilize guidelines and protocols for these types of critically ill children understanding that the uniqueness of each child can create different responses
- Participate in individual approach to each of the three cases for management and treatment.

Let's set the stage...

- You come on and get sign out to include
  - A 17 year-old female with ingestion, intubated
  - A 5 year-old female with traumatic brain injury (TBI)
  - A 17 month-old female, s/p laryngotracheal reconstruction (LTR)

Case # 1

- 17 year-old female admitted to the PICU after ingesting
  - Diltiazem
  - Metformin
  - Compazine
  - Oxycodone
- Concern for
  - Severe hypotension
  - Altered mental status
- History
  - Patient presented to outside hospital with c/o of nausea and vomiting, having ingested unknown amounts of medication
  - Patient is healthy but for new diagnosis of bulimia
  - Mother states this could have been trigger for ingestion
Case #1

- Past medical history
  - None
- Past surgical history
  - None
- Medications
  - None
- Allergies
  - None

Patient blood pressure in emergency department = 70/30
- 5 fluid boluses of NS given
- Norepinephrine infusion started
- Abnormal labs:
  - Elevated creatinine: 1.4
  - Lactic acid: 9
- All other labs were within normal limits
- Blood pressure improved to 80/30 with norepinephrine infusion @ 1 mcg/kg/min
- Dopamine infusion was started @ 15 mcg/kg/min
- Foley was placed with UOP normal for age

What do we know about Diltiazem?
- Diltiazem
  - Calcium channel blocker
  - Antagonist at L-type voltage-sensitive calcium channels in the myocardium, vascular bed and pancreas
  - Blocks influx of calcium to the cell
  - Limiting release of calcium stored in sarcoplasmic reticulum
  - Disruption of calcium homeostasis
  - Negative chronotropic and inotropic effect
  - Vasodilation
  - Impaired glucose metabolism
- OVERDOSE
  - Bradycardia, hypotension, hyperglycemia
  - Typically effects several hours after ingestion
  - 18 to 24 hours
  - REFRACTORY to standard therapies

What about Compazine and Metformin?
- Compazine
  - Used as antiemetic; antipsychotic; migraine headache
  - Blocks postsynaptic mesolimbic dopaminergic receptors in brain
  - Medullary chemoreceptor trigger zone
  - Alpha adrenergic block
  - Depression of hypothalamic hormones
  - Respiratory depression
  - Lowered seizure threshold
  - Anticholinergic effects
  - Depression of hypothalamic hormones
  - Reprocess, QRS prolongation
  - Metformin
  - Reduces hepatic glucose production; improves insulin sensitivity
  - Hypoglycemia
  - Lactic acidosis
  - Impaired renal function

Case #1 progression
- CVS – added epinephrine infusion
  - Developed prolonged QTC
  - Serial EKG’s
- RESP: intubated for acute encephalopathy
- Neuro
  - Ativan on call for seizures
  - Fentanyl infusion for analgesia
- Endocrine
  - Stress dose steroids

How does one “pick” their first line of vaso-actives?
- A. PALs protocol tells us what to use
- B. Decide what is needed - + chronotropy or + inotropy or both
- C. Always use just one vaso-active so as not to confuse the situation
Review

• Alpha 1 – Vasculature \(\rightarrow\) Tightens vessels
• Beta 1 – Myocardium \(\rightarrow\) Increases HR and squeeze
• Beta 2 – Vasculature \(\rightarrow\) Dilates vessels

What therapies are available?

• Conventional
  • Inotropic agents
  • Vasopressors
  • BOTH INCREASE SYSTEMIC VASCULAR RESISTANCE AND MYOCARDIAL OXYGEN DEMAND
• High-dose Insulin/Glucose therapy
  • Mechanisms to reverse cardiotoxic poisoning
  • Positive inotropy: possible effect of insulin on glucose metabolism
  • Vasodilatation: insulin dilates peripheral vessels
  • Metabolic effects: Calcium channel blocker poisoning will increase insulin release from pancreas with ensuing hyperglycemia
  • Decreased insulin release prevents glucose utilisation
  • Physiologic effects: to increase blood pressure and tissue perfusion
  • Dilating peripheral vasculature
  • Increasing myocardial uptake of glucose
  • Providing heart with energy source
  • Acting as positive inotropic agent

High-dose insulin/glucose therapy

• Effective
• Documented in tissue and animal experiments
• Still not proven as to whether mechanisms truly contribute to therapeutic effects
  • Holger et al: 12 patients treated; 11/12 survived
  • Issues with ingestions of multiple drugs, interpretation of results is challenging
  • Greene et al and Shah et al: show many case reports of high-dose insulin/glucose therapy with overall 80% survival
• No clinical trials have been done to evaluate effectiveness for severely poisoned patients
  • Requirements for use not established
  • Which patients will benefit
  • Proper dosing
  • When to start and stop treatment
  • Adverse effects
  • Monitoring parameters
  • How intervention will be affected by other drugs or therapies in use

Case #1

• Patient developed AKI related to hypotension
  • Concern for further renal damage
  • Placed on CRRT for 2 days
  • UOP returned to normal with normalization of electrolytes, BUN and creatinine
  • Prolonged QTc resolved without need for imaging of the heart
  • Extubated 3 days after admission without any sequelae

Fluid Balance

- Goals should be to prevent > 10% fluid overload
- Diuretics when shock resolved
  - +/- Albumin
- CRRT - A slow continuous fluid removal that can use both diffusion and convection to remove fluid and solutes
Propofol Infusion Syndrome: Risk Factors

Through evaluation of the case reports and case series, there appears to be several trends for Risk Factors (although there are also outliers). [Diedrich, 2011; Okamoto, 2005]

- Dose of Propofol >1 mg/kg/hr
- Duration of Propofol infusion 6 hours or greater
- Patients with Ion Elaborations of Metabolism
- Concurrent infusion of Vasopressors
- Concurrent use of Thrombolytics
- Patients with "Critical Illness"
- "Younger" Age – although death seemed to more likely occur in patients >18 years of age.

Questions we all have about initial treatment of TBI

- Do all TBI patients need to be
  - mechanically ventilated?
  - have ICP monitors?
  - have arterial and central line catheters?
  - serial head CT scans?
- What are the key signs of herniation?
  - Pupillary dilation
  - Bradycardia
  - Bradypnea
  - (hard to tell when mechanically ventilated)
  - Hypertension
  - Possibly obscured by sedation
  - Unilateral/bilateral weakness
  - Dysrhythmias
  - Decerebrate/decorticate posturing
  - ICP – “spike” = medical emergency

Why do we limit the use of Propofol in children?

- Propofol Infusion Syndrome
  - Very rare, but deadly complication associated with Propofol administration.
  - May be an extreme manifestation of a more common and initially reversible physiologic state. [Diedrich, 2011]
  - Causation or mechanism has, as yet, not been determined.

- Clinical Features: [Diedrich, 2011]
  - Cardiovascular
    - Hypertension
    - Hypotension (es, Bradycardia, Wide QRS, Brugada‐like ECG, VTach, PEA, asystole)
  - Hemorrhagic
  - Hyperthermia
  - Hemoglobin and Transaminitis
  - Hyperglycemia and hyperlipidemia
  - Hepatic
  - Renal and Metabolic
    - Rhabdomyolysis
    - Myocardial Failure
  - Neurological
    - Decorticate/decerebrate posturing
    - Unilateral/bilateral weakness
  - Brainstem impaintment
  - Bradycardia
  - Bradypnea
  - Brainstem (es, Bradycardia, Wide QRS, Brugada‐like ECG, VTach, PEA, asystole)

- Propofol Infusion Syndrome: Risk Factors

- What are the key signs of herniation?
  - Pupillary dilation
  - Bradycardia
  - Bradypnea
  - (hard to tell when mechanically ventilated)

- Hypertension
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  - Unilateral/bilateral weakness
  - Dysrhythmias
  - Decerebrate/decorticate posturing
  - ICP – “spike” = medical emergency

What are we gonna do? Follow TBI Guidelines – Consensus 2019

- Third edition of guidelines for management of Pediatric Severe Traumatic Brain Injury (TBI) [Kochanek PM et al. Mar 2019; www.pccmjournal.org; Vol 20;3]
  - Evidenced based recommendations for Treatment
  - Allows for most optimal treatment regimen
  - Algorithm approach
    - Synthesis of evidence and consensus-based assistance to clinical decision-making
    - Specifics to direct care
    - Many available treatment options
    - Still work in progress for hopes for standardization in future
    - Use of minimum therapeutic targets
      - ICP, CPP
  - Allows for individualization within context of response to various therapies
    - Integration of all available information
    - Use of pathway and guidelines

Case # 2

- 5 year-old female who sustained penetrating head trauma when a 20 pound call ornament with metal spike fell and pierced the top of her head.
- She was taken to hospital by EMS
- Ornament fell out of her head
- Intubated at hospital for airway protection
- Ceftriaxone administered
- Given 5ml/kg of HTS
- Replaced with morphine and pentobarbital infusions
- Paralytic infusion started
- Repeated with morphine and pentobarbital infusions
- Burst suppression of seizures (none seen on continuous EEG)
- Analgesia
- Multi‐tasking
- Very rare, but deadly
- "Propofol Infusion Syndrome"
  - Why do we limit the use of Propofol in children?
  - What are we gonna do? Follow TBI Guidelines – Consensus 2019
  - Questions we all have about initial treatment of TBI
  - Why do we limit the use of Propofol in children?
Treatment of brainstem herniation

- Don’t wait for
  - CT
  - Neurosurgery
- FiO2 >1.00
- Titrate to pupillary response
- Administration of
  - Mannitol: > 0.5 - 1 gram/kg (maximum dose of 30 ml) over 10 minutes
  - Hypertonic saline (3%): > 1 - 3 ml/kg, (maximum dose of 250 ml) over 10 minutes
  - Or 23.4%: > 0.5 ml/kg (maximum dose of 30 ml) over 10 minutes
- Maintain hemodynamic stability
- EVD – if in place, open and lower to 0 cm above tragus

Baseline Care for TBI

- Maintenance of appropriate level of analgesia and sedation
- Benzodiazepine + opioid
- Midazolam + Fentanyl/morphine
- Controlled Mechanical Ventilation
- Titration of FiO2 to achieve saturations >92% PaO2 75 - > 100 mmHg
- PEEP 5-10 and <10 cm H2O
- CO2 25-40 mmHg
- Maintaining Normothermic Core Temperature AND Preventing/Treating fever
  - >35 and <38 degrees C
- Insuring appropriate Intravascular Volume Status
  - Euvolemia
    - CVP >4 and <10 mmHg
    - UOP >1 ml/kg/hr
    - NS
  - Na 135 - 150 mEq/dL* exceptions with hyperosmolar therapy
  - 5% dextrose to avoid hypoglycemia
  - Maintain glucose <180 mg/dL
  - Nutritional support as soon as possible

More Baseline Care for TBI

- Maintaining Minimum Blood Hemoglobin
  - Target >7 g/dl
- Treatment of Coagulopathy
  - Aim for INR of <1.5
  - Attention paid to insertion of ICP monitor or surgery
- Neutral Head Positioning with Head-of-Bed Elevation
  - Midline
  - 30 degrees head-of-bed elevation
  - Antiepileptic Drug Therapy and Use of Continuous Electroencephalography
  - No consensus
  - Levetiracetam easiest

Case #2

- Brain CT post 24 hours of injury showed increase in hemorrhage
- Arteriogram with R ACA embolization
- Dexamethasone initiated
- Continued elevated ICPs
- Bilateral craniotomies performed with hematoma evacuation
- Weaned off HTS and then restarted
- Bone flap removal with improved cerebral edema
- Slow wean of pentobarbital, HTS and morphine infusions
- Due to sodium fluctuations, TPN started
- Trophic feeds slowly advanced
- Intermittent ileus and resolved

Structures Supplying Blood Flow to the Brain

- Two internal carotid arteries anteriorly
- Vertebral arteries posteriorly

Role of corticosteroids in TBI?

- Mechanisms of corticosteroid function
  - Is most efficacious against inflammation related to vasogenic edema but not cytotoxic edema
  - The efficacy of corticosteroids against tumor-related vasogenic edema is undisputed.
  - We routinely observe brain tumor patients with deficit attributable to vasogenic edema to improve after corticosteroid administration.
  - These observations contrasts those in the TBI or traumatic spinal cord injury patients, where cytotoxic edema predominates.
  - It remains unclear whether the pathophysiology processes in a subset of TBI patients involve vasogenic edema.
- Vasogenic edema is defined as extracellular accumulation of fluid resulting from disruption of the blood-brain barrier (BBB) and extravagations of serum proteins, while cytotoxic edema is characterized by cell swelling caused by intracellular accumulation of fluid.
What is the purpose of dexamethasone in TBI?

• Multicenter, double-blinded, placebo-controlled RCT
• 10,008 patients with head injuries and GCS < 14
• Either 48 hour infusion of methylprednisolone (2 g for 1 hour followed by 4 mg for 48 hours) or placebo
• Primary outcome included death within 2 weeks
• No significant differences were noted between both arms
• 94% of the enrolled patients were available for the 6-month follow-up
• 1008 patients with head injuries and GCS < 14
• Multicenter, double-blinded, placebo controlled RCT
• Risk of death within 2 weeks of entering the study was higher in the corticosteroid arm (21.3% vs 17.9%, \( P = 0.001 \))
• 94% of the enrolled patients were available for the 6-month follow-up
• The 6-month mortality was higher in the steroid-treated arm relative to the placebo arm (25.7% vs 22.3%, \( P = 0.001 \))
• No significant differences were noted between both the study arms in terms of 6-month disability and TBI-related complications were comparable between the two arms.

ICP management in TBI

• ICP Target value <15 mmHg and no more than 25 mmHg
• Can use PibO2 level (jugular vein saturation (SjO2)) and accept levels between 20 and 25 mmHg or 55% - 75%
• EVD between 3-5 mmHg or up to 27.2 cm H2O above tragus
• Intervene after 5-30 minutes of elevation
• Progression
  - EVD drainage > HTS bolus
  - Hold HTS if platelet count <100 X10³ or INR >1.4 or creatinine rise 24 baseline
  - For additional spikes
  - Continue HTS bolus or increasing infusion
  - Monitor volume status and constellarity
  - >300 mL/h
  - Consider additional analgesia/edenture
  - Muscular blockade

Case # 2

• Inotropic infusions weaned
• Hypertension persisted
• Antibiotics/antibiotic started
• Transfused PRBCs initially
  - Prolonged INR led to Vitamin K therapy
  - Developed RLE venous thrombosis
  - Re imaging of head showed no clot
  - Started heparin infusion and transitioned to enoxaparin
  - Antibiotics initially CTX/Vancomycin
  - Added flagyl
  - Switched from CTX to cefazdime to cefepime
• Multiple episodes of fever with sepsis profile
• Developed lactobacillus related to gut translocation and started on ampicillin


What is the risk of hypertension with TBI?

• Pathophysiologic impact of hypertension is complex
  - Involves the interplay between systemic blood pressure and cerebral autoregulation
  - In the non-injured brain, pre- or postcapillary autoregulatory mechanisms maintain a constant cerebral blood flow, despite large changes in systemic blood pressure
  - First phase when systemic blood pressure is reduced
  - Increase in IC P
  - CPP initially decreases
  - Second phase as CPP continues to rise
  - Systemic blood pressure then increases to re-establish normal CPP
  - Progressive autoregulatory vasodilatation stabilizes the balance between systemic blood pressure and CPP
  - Injury brain
    - Autoregulatory vasodilatation may be impaired
    - Increased IC P
    - Breakdown of the blood–brain barrier
    - May cause increased regional cerebral blood flow and transudation of fluid across the disrupted blood–brain barrier
    - Increased cerebral edema and intracranial pressure and result in cerebral edema

Therapies often improve one thing and worsen another...

- Treatment of CPP with vasopressor with patient with impaired BP autoregulation of CBF
  - Increase in CBV will worsen ICP
- Treatment of MAP with BP autoregulation preserves CBF
  - Reduces CBV and then reduces ICP

When first tier management is inadequate and ICP keeps going up—second tier therapies

- CT repeat
  - Expanding lesion / diffuse swelling
- Neurosurgical options
  - Decompressive craniectomy
    - With or without duraplasty
    - With or without evacuation of hematoma
- Barbiturate infusion
  - Failure of osmotherapy and hyperventilation to keep ICP <25 mmHg
  - Increase infusion and ICP <25 mmHg and then start to decrease
  - Aim to withdraw infusion over 24-96 hours
  - Vasopressor often needed to maintain adequate CPP
- Moderate Hypothermia for refractory intracranial hypertension
  - Target temperature 32-33°C
- Induced Hyperventilation and hyperosmolar therapies
  - Combinations of gradations of hypocapnia (28 to 34 mmHg PCO2) with Na+2 levels between 155-160 mEq/L with osmolarity between 320 and 240 mOsm/L with pentobarbital infusion at rate of 2-4 mg/kg/hr

Advanced monitoring

- All used to optimize
  - Titration of therapies
    - Pbro2
      - Monitoring can determine whether hyperventilation is producing reductions in tissue oxygenation
    - cEEG
      - Recognizing subclinical status epileptics is contributing to increased intracranial pressure
    - Transcranial Doppler ultrasound
      - Assessing CBF velocity to ischemic areas when hyperventilation is escalated

How to withdraw therapies

- Go in reverse order of application
- Duration of stability
  - 12-24 hours
  - Second tier often takes longer to withdraw than first tier
- Neurologic exam helps guide withdrawal of therapies

What? NO ICP monitor?

- Research is lacking
- Serial CT imaging
  - 48 hours after injury
  - 5-7 days after injury
- Pupillary exam

Case # 3

- 17 month-old female, ex-25 week, with subglottic stenosis, s/p laryngotracheal reconstruction with rib graft and left vocal cord innervation; CLD, tracheostomy dependence, s/p PDA ligation, admitted to PICU for respiratory support in setting of hypoxic/hypercarbic respiratory failure.
- Past medical history
  - Premature (25 weeks); subglottic stenosis, CLD, GERO, G-tube dependence, PDA l/s ligation
- Surgical history: tracheostomy, G-tube
- Social history – lives with mother and father; no smokers
- Medications- lansoprazole; albuterol and Pulmicort
- Allergies – none
Case #3

- Initially, intubated following LTR protocol
- DLB performed 8 days after surgery showed mucosalized anterior and posterior grafts
- Persistent stridor necessitated balloon dilation for tracheal stenosis 4 and 1/2 weeks after initial LTR
  - Granulation tissue visualized lateral to graft with prolapse
- Laryngotraceoplasty with tragal cartilage performed 4 weeks after initial surgery
- Respiratory
  - Maintained on minimal ventilatory settings and extubated 3 weeks after initial LTR
  - Required reintubation with quick extubation 4 weeks post LTR to HFNC and helenox
  - Developed distress and was reintubated
- Extubated to HFNC 6 weeks after initial LTR

Why is sedation such a nightmare?

- Adequate and appropriate sedation for mechanically ventilated children is a challenge
- Essential to keep children safe and comfortable
  - Reduces pain, anxiety, agitation, and physiologic stress response that mechanical ventilation, invasive monitors and devices
  - Worrisome data about "excessive sedation is detrimental"
  - Longer MV days
  - Longer ICU/hospital stays
  - Higher costs
  - Impact on "prime of cognitive development" may lead to "permanent alterations in neurologic function".

In children with opioid infusions, when can you expect to "double" their dosing?

- A. < 1 day
- B. < 3 days
- C. < 5 days
- D. < 7 days

Sedation/Analgesia trends in PICU

- Widespread variation of
  - Opioid infusions,
  - Benzodiazepine infusions
  - Neuro-muscular blocking agents
  - All attempting to mitigate sedation withdrawal with
    - Enteral agents
    - Intravenous bolus vs. infusions
    - Intermittently suspending infusions
    - Allowing for metabolic clearance
- Martin et al., 2001; Rhoney and Murray, 2002; Jenkins et al., 2007

Nightmare continues....

- Approaches to management of sedation dependent on
  - Physician preference
  - Resources
  - Nursing staff assessments
  - PICU protocols have shown variable success
  - Randomized clinical trial showed no difference in duration of mechanical ventilation but less days of opioid administration and less exposure to fewer sedative classes
  - Kids were often awake and calm when intubated
  - Systematic review of six observational studies addressing PICU sedation showed association between
    - Guidelines
    - Protocols
    - Algorithms
    - Reduced PICU LOS, sedation duration and dose and prevalence of drug withdrawal
A sedation protocol aims to...

• Deliver adequate sedation and analgesia with purpose of keeping patients safe and comfortable
• Reducing pain, anxiety, agitation, and physiologic stress response
  • Airway control
  • Ventilator synchrony
  • Hemodynamic stability
  • Tolerating invasive monitoring and procedures
  • Minimizing oxygen consumption and metabolic demands
• Use the minimal amount of opioid and/or benzodiazepine necessary
• We all try to avoid withdrawal

Patient appears uncomfortable. Is the patient in pain?

Morphine 0.05‐0.1 mg/kg/dose (usual starting max: 5 mg/dose) IV every 10 minutes until desired pain score achieved. Max 3 doses.

Yes

Patient scores more positive than desired MMAAS. Reversible causes of agitation have been excluded. Environmental comfort measures provided but increased state of behavior is causing acute deterioration in patient’s condition necessitating immediate control.

No

Midazolam 0.05‐0.1 mg/kg/dose (usual max starting dose: 4 mg/dose) IV every 10 minutes until desired MMAAS score achieved. Max 3 doses.

Anticipated length of intubation?

Less than or equal to 48 hours?

Greater than 48 hours?

For pain INTERMITTENT DOSES

CONTINUOUS INFUSIONS

For sedation/agitation

Morphine infusion 0.05 mg/kg/hr (usual starting max: 4 mg/hr) AND

Midazolam infusion 0.05 mg/kg/hr (usual starting max: 2 mg/hr) AND

Docusate 2.5 mg/kg/dose (adult dose: 250 mg/dose) PO/Tube BID

Bolus and/or pre‐care doses are the same 1 hour dosing of morphine and midazolam drips

Midazolam 0.05‐0.1 mg/kg/dose (usual starting max: 4 mg/dose) IV every 2 hours PRN agitation. Can consider dexmedetomidine continuous infusion.

Morphine 0.05‐0.1 mg/kg/dose (usual starting max: 5 mg/dose) IV every 2 hours PRN pain.

Consider reversible causes of agitation and non‐pharmacologic means to decrease agitation.

Consider reversible causes of pain and non‐pharmacologic means to decrease pain.

A little pharmacology/physiology

• Opioids receptors
  • Produce analgesia through inhibition of synaptic transmission
  • Chronic stimulation leads to desensitization
  • Tolerance develops
    • Cessation of opioid
      • Rebound increase in neurotransmitter release
        • HYPEREXCITABILITY OF BRAIN REGIONS
  • Benzodiazepine receptors
    • Modulation of GABA‐A receptors
    • Hyperpolarization leads to sedation and anxiolysis
    • Withdrawal
      • Decreases efficacy of available GABA at receptor sites
      • Leads to inhibition of central nervous system

A little pharmacology/physiology

• Long term physiological consequences of drug exposure in critical illness
  • Cardio‐respiratory derangements
  • Blunted counter‐regulatory neuroendocrine and stress responses
  • Tolerance, dependence, addiction and withdrawal
    • Neurocognitive and developmental delay
      • Developing brains are about proliferating and migrating
        • Affected by GABA agonists – opioids and benzodiazepines
        • Affected by NMDA antagonist – ketamine
        • Dexmedetomidine – an alpha 2 agonist – not enough studies to know
        • Bradycardia and hypotension
        • Decreased spatial and verbal memory and sustained attention
        • Impaired executive function – area of brain responsible for purposeful, goal‐directed, and problem solving behavior required for higher learning

And, so we have learning a few things about sedation...

• Tolerance
  • Development of a need to increase dose of opioid or benzodiazepine agonist to achieve the same analgesic or sedative effect previously achieved with lower dose

• Physical dependence
  • Caused by repeated administration of opioid
  • Necessitates continued administration of drug to prevent appearance of withdrawal
  • Usually occurs after 2‐3 weeks of morphine administration, but can occur sooner

Just a review...

• Tolerance

• Physical dependence

How widely are sedation protocols used in the pediatric critical care setting?

• A. Rarely
• B. About 25 % of the time
• C. Barely 50% of the time
• D. About 75% of the time
State of Pediatric Critical Care Sedation/Analgesia Practices

• Online survey members of World Federation of Pediatric Intensive care and Critical Care Societies*
  • <30% respondents had written protocols
  • 52% Physician-led protocols
  • North American: 58% Nurse-led protocols
  • 70% report using scoring system
  • 42% use it on as daily patient-care goal basis

Kudchadkar SR et al. Crit Care Med 2014 (42)

Are there any “set” doses of opioids/benzodiazepines that are associated with withdrawal?

• Yes
• No

• NO study has established total morphine doses associated with withdrawal
• We just use what it takes and keeps the kid safe
• Lack of standardized and validated tool for iatrogenic withdrawal in PICU is a problem
  • Different age
  • Developmental levels

And then there is delirium...

• Acute and fluctuating disturbance of consciousness and cognition
• Neuropsychiatric symptoms
  • Attention
  • Awareness
  • Behavior
  • Cognition
  • Perception
• Risk factors
  • < 5 years of age
  • Developmental delay
  • Increased illness severity: the sicker the kid,
  • Mechanical ventilation: 2/3 of patients admitted to PICU

Delirium Screening: The P-CAM ICU

Why do we worry about delirium?

• Short and long term physiologic consequences of drug exposure in critical illness
• Cardio-respiratory derangements
• Blunted counter-regulatory neuroendocrine and stress exposures
• Neurodevelopmental delay
• Tolerance, physical dependence, addiction and withdrawal
• Delirium is often a by-product of sedation
  • 72% of pediatric intensivists use combination of opioids and benzodiazepines as sedation regimen
**Risk Factors for Pediatric Delirium**

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<th>Predisposing Risk Factors</th>
<th>Precipitating Risk Factors</th>
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<td>Developmental Delay</td>
<td>Benzodiazepines</td>
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<td>High Severity of Illness</td>
<td>Cardiac Bypass Surgery</td>
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<td>Low Albumin &lt;3 mg/dl</td>
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<td>Pre-Existing Medical Condition</td>
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<td>RACHS Score &gt; 2</td>
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<tr>
<td>Cyanotic Heart Disease</td>
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**Conclusions**

- Therapies for complex ingestions require more study
  - Talk to Poison Control for most up to date guidelines

- Use the 2019 Guideline for pediatric TBI
  - Algorithm allows for individual but carefully supported care

- Sedation of the pediatric patient continues to be a challenge
  - Protocols need to be used consistently so that patterns can encourage change