Sedation And Analgesia In Pediatric ICU

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Pediatric Intensivist
Outlines

- Introduction
- Goals
- Definitions
- The challenges of PICU sedation
- Sedation & Analgesia monitoring
- Medications options
- Suggested strategies
- Precautions
- Conclusion & key points
PICU Experience

- Physical Pain
  - Primary disease
  - Surgical treatment or traumatic event
  - Procedure (Central line insertion)
  - ET tube presence for MV
PICU Experience

• Separation from family
• Disturbed sleep cycle
• Noise (machines)
• Fear of death
• Loss of self-control
😊 Problem Solved 😊
Why Do We Need IT?

- **Benefits:**
  - Decrease child anxiety and pain
  - Facilitate care
  - Safety

- **Risks:**
  - Prolonged MV with its complications
  - Withdrawal syndrome
ICU Without S&A

- A metabolic, humoral, and hemodynamic response following injury or surgery

- This neuro-endocrine cascade leads to:
  - increased oxygen consumption
  - increased carbon dioxide production
  - a generalized catabolic state with a negative nitrogen balance
Goals

- Patient comfort
- Control of pain
- Anxiolysis
- Amnesia
- Blunting adverse autonomic and hemodynamic responses
- Facilitate nursing management
- Facilitate mechanical ventilation
- Avoid self-extubation or self injury
- Reduce oxygen consumption
Definitions
**Sedation:** The act of calming, especially by the administration of a sedative.

**Analgesia:** A condition in which nociceptive stimuli are perceived but are not interpreted as pain. Usually accompanied by sedation without loss of consciousness.

*Sedation ≠ Analgesia*
Continuum of Consciousness

Awake, baseline  Moderate sedation  General anesthesia

Minimal sedation  Deep sedation
Definitions (Level of Sedation)

• **Minimal Sedation (anxiolysis)**
  ◦ Responds to verbal commands
  ◦ Cognitive function and coordination may be impaired
  ◦ Ventilatory and Cardiovascular not affected

• **Moderate**
  ◦ Responds to verbal comments alone or accompanied by touch.
  ◦ Maintain airway, ventilation and cardiovascular.
Deep
- Cannot be easily aroused but responds to noxious stimuli.
- May require assistance to maintain airway and adequate ventilation, cardiovascular maintained

General Anesthesia
- Patient cannot be aroused.
- Often requires assistance to maintain airway and positive pressure ventilation.
- Cardiovascular status may be impaired.
The Challenges of PICU Sedation
Assessment of sedation
Altered pharmacology
Tolerance
Delayed emergence
Withdrawal
Drug interaction
Sedation Balance

Causes for Agitation

Sedatives
Causes for Agitation

- Agitation & anxiety
- Pain and discomfort
- Catheter displacement
- Inadequate ventilation
- Hypertension
- Tachycardia
- Arrhythmias
- Wound disruption
- Patient injury

Sedatives
Sedatives

Causes for Agitation

- Prolonged sedation
- Delayed emergence
- Respiratory depression
- Hypotension
- Bradycardia
- Increased protein breakdown
- Muscle atrophy
- Venous stasis
- Pressure injury
- Loss of patient-staff interaction
- Increased cost
Correctable Causes of Agitation

- Full bladder
- Uncomfortable bed position
- Inadequate ventilator flow rates
- Mental illness
- Uremia
- Drug side effects
- Disorientation
- Sleep deprivation
- Noise
- Inability to communicate
Causes of Agitation
Not to be Overlooked

• Hypoxia
• Hypercarbia
• Hypoglycemia
• Endotracheal tube malposition
• Pneumothorax
• Abdominal pain
• Drug withdrawal
Sedation Scoring Scales

- Ramsay Sedation Scale (RSS)
- Sedation-agitation Scale (SAS)
- Observers Assessment of Alertness/Sedation Scale (OAASS)
- Motor Activity Assessment Scale (MAAS)

*BMJ 1974;2:656-659*
*Crit Care Med 1999;27:1325-1329*
*J Clin Psychopharmacol 1990;10:244-251*
*Crit Care Med 1999;27:1271-1275*
Challenges in PICU

Behavioral clues to pain or anxiety are often difficult to differentiate
Facts about Pain in Infants and Children

- Even premature infants have the anatomic and physiologic components to perceive pain.
- They demonstrate a severe stress response to painful stimuli.
- Complete myelination of nerve pathways is not required for pain transmission.
- Inhibitory pathways do not develop until after birth (more sensitive).
Children Do Not Tolerate Pain Better Than Adults

- Children’s tolerance to pain actually increases with age.
- Children beyond infancy can accurately point to the body area or mark the painful site on a drawing.
Children as young as 3 years can use pain scales.
Photographic/ Numeric Pain Scale
(Oucher scale) --->

- BROWS: lowered, drawn together
- FOREHEAD: bulge between brows, vertical furrows
- EYES: tightly closed
- NOSE: broadened, bulging
- MOUTH: open, squarish
Wong Baker Faces
3 Years and above

Ask the child to pick the face that best describes how much hurt or pain he/she has. Explain the faces and point to each one as you say the words shown beneath the face.
## CRIES Pain Scale 0-6 months

<table>
<thead>
<tr>
<th></th>
<th>0</th>
<th>1</th>
<th>2</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Crying</strong></td>
<td>No cry or cry that is not high-pitched</td>
<td>Cry high pitched but baby is easily consolable</td>
<td>Cry high pitched but baby is inconsolable</td>
</tr>
<tr>
<td><strong>Requires O2 for SaO2 &lt;95%</strong></td>
<td>No oxygen required</td>
<td>&lt;30% oxygen required</td>
<td>&gt;30% oxygen required</td>
</tr>
<tr>
<td><em><em>Increased vital signs (BP</em> and HR</em>)**</td>
<td>Both HR and BP unchanged or less than baseline</td>
<td>HR or BP increased but increase in &lt;20% of baseline</td>
<td>HR or BP is increased &gt;20% over baseline</td>
</tr>
<tr>
<td><strong>Expression</strong></td>
<td>No grimace present</td>
<td>Grimace alone is present</td>
<td>Grimace and non-cry vocalization grunt is present</td>
</tr>
<tr>
<td><strong>Sleepless</strong></td>
<td>Child has been continuously asleep</td>
<td>Child has awakened at frequent intervals</td>
<td>Child has been awake constantly</td>
</tr>
</tbody>
</table>
Physiological Indications of Acute Pain

- Dilated pupils
- Increased perspiration
- Increased rate/force of heart rate
- Increased rate/depth of respirations
- Increased blood pressure
- Decreased urine output
- Decreased peristalsis of GI tract
- Increased basal metabolic rate
Multidimensional Model of Pain Assessment

Vocal
- Self reporting
- Cry, scream, groan

Physiologic
- VS
- O₂ changes
- Hormonal changes
- Sweating

Pain Assessment Clues
- Pain stimulus/Hx
- Temperament
- Age, Sex
- Culture

Behavioral
- Facial expression
- Posture
- Activity
- Behavioral state
- Response to intervention

Contextual
The Golden Rule

What is painful to an adult is painful to an infant and child
Observe for Improvement in Behavior Following an Analgesic
## FLACC (0-8 Years)

<table>
<thead>
<tr>
<th></th>
<th>0</th>
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<th>2</th>
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</thead>
<tbody>
<tr>
<td><strong>Face</strong></td>
<td>No particular expression or smile. Relaxed face, makes eye contact, shows interest in surroundings</td>
<td>Occasional grimace or frown, withdrawn, disinterested Worried facial expression, eyebrows lowered, eyes partially closed, cheeks raised, mouth pursed</td>
<td>Frequent to constant frown, quivering chin, clenched jaw Deep furrows in forehead, closed eyes, open mouth, deep lines around nose and lips</td>
</tr>
<tr>
<td><strong>Legs</strong></td>
<td>Normal position or relaxed Normal muscle tone and motion in limbs</td>
<td>Uneasy, restless, tense Increased tone, rigidity, or tension Intermittent flexion or extension of limbs</td>
<td>Kicking, or legs drawn up Hypertonic; legs pulled tight, exaggerated flexion or extension of limbs, tremors</td>
</tr>
<tr>
<td><strong>Activity</strong></td>
<td>Lying quietly, normal position, moves easily Normal activity/restrictions</td>
<td>Squirming, shifting back and forth, tense torso Hesitant to move, guarding, demonstrates pressure on a body part</td>
<td>Arched, rigid or jerking In a fixed position, rocking, side-to-side head movement, rubbing a body part</td>
</tr>
<tr>
<td><strong>Cry</strong></td>
<td>No cry or moan (awake or asleep)</td>
<td>Occasional moans, cries, whimpers, sighs</td>
<td>Crying steadily, screams or sobs, Frequent or continuous moans, cries, grunts</td>
</tr>
<tr>
<td><strong>Consolability</strong></td>
<td>Content, relaxed Calm, does not require consoling</td>
<td>Reassured by occasional touching, hugging or being talked to, distractible Responds to comfort by touching or talking in 30 sec. to 1 min.</td>
<td>Difficult to console or comfort, requires constant comforting, inconsolable</td>
</tr>
</tbody>
</table>
## COMFORT SCALE SCORE

**Intubated, Non-paralyzed patients**
*(Target Range 17-26)*

<table>
<thead>
<tr>
<th></th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Alert</strong></td>
<td>Deeply Asleep</td>
<td>Lightly Asleep</td>
<td>Drowsy</td>
<td>Alert &amp; Awake</td>
<td>Hyper Alert</td>
</tr>
<tr>
<td><strong>Calmness</strong></td>
<td>calm</td>
<td>Slightly Anxious</td>
<td>Anxious</td>
<td>Very anxious</td>
<td>Panicky</td>
</tr>
<tr>
<td><strong>Respiratory Response</strong></td>
<td>No cough or spontaneous respirations</td>
<td>spontaneous respirations</td>
<td>Occasional cough or breaths out of synchrony with vent</td>
<td>Actively breaths against the vent or cough regularly</td>
<td>Fights ventilator; cough or choking</td>
</tr>
<tr>
<td><strong>Physical Movement</strong></td>
<td>none</td>
<td>Occasional slight movement</td>
<td>Frequent slight movement</td>
<td>Vigorous movement</td>
<td>Vigorous movement of head &amp; torso</td>
</tr>
<tr>
<td><strong>Blood Pressure</strong></td>
<td>Below baseline</td>
<td>Consistently at baseline</td>
<td>Infrequent (1-3) elevation of 15% / more</td>
<td>frequent (&gt;3) elevation of 15% / more</td>
<td>Sustained elevation&gt; or =15%above the baseline</td>
</tr>
<tr>
<td><strong>Heart Rate</strong></td>
<td>Below baseline</td>
<td>Heart rate at baseline</td>
<td>Infrequent (1-3) elevation of 15% / more</td>
<td>frequent (&gt;3) elevation of 15% / more</td>
<td>Sustained elevation&gt; or =15%above the baseline</td>
</tr>
<tr>
<td><strong>Muscle Tone</strong></td>
<td>Relaxed/ no muscle tone</td>
<td>Reduced Muscle tone</td>
<td>Normal muscle tone</td>
<td>Increased muscle tone</td>
<td>Extreme muscle rigidity</td>
</tr>
<tr>
<td><strong>Facial Muscle</strong></td>
<td>Relaxed / no facial muscle tone</td>
<td>Normal facial tone</td>
<td>Some tension in brow, forehead or mouth</td>
<td>Full facial tension</td>
<td>Facial muscles contorted</td>
</tr>
</tbody>
</table>
State Behavioral Scale score

Patient’s response to voice, then gentle touch, then noxious stimuli “planned endotracheal suctioning or < 5 seconds of nail-bed pressure”

-3 $\rightarrow$ 0 $\rightarrow$ +3
BIS Monitoring

For objective sedation measurement.
Awake

- Responds to normal voice

80

- Responds to loud commands or mild prodding/shaking

60

- Low probability of explicit recall
- Unresponsive to verbal stimulus

40

20

- Burst suppression

0

Flat Line EEG
Altered Pharmacology in PICU Setting
Physiologic Changes That Affect Pharmacokinetics in PICU Patient

- Unstable patients often present with significant hemodynamic alterations and organ dysfunction, which may significantly alter drug:
  - Absorption
  - Transport
  - Metabolism
  - Excretion
Absorption

- Altered GI motility and peristalsis (ileus, recent GI surgery)
- Reduced gut function and absorptive surface area (pancreatitis, recent GI surgery)
- Reduced GI blood flow (shock)
- Physical removal of drug by nasogastric suctioning.
Other Routes

- Parenteral (IV, IM, SQ) drug administration is most common in the critically ill.
- Drug absorption may be decreased due to decreased tissue perfusion and decreased movement of drug through edematous tissue.
- Transdermal route may become useful (e.g., using fentanyl, clonidine)
Distribution

- Poor perfusion is often a factor that limits distribution of a drug to its target tissue.
- Many analgesic drugs are transported attached to the serum proteins.
- The extent of protein binding may decrease in critical illness, causing elevated free levels of drug and possible toxicity.
- Third-spacing of fluid may result in additional volume into which the drug can distribute.
Metabolism and Elimination

- It is common for ICU patients to have some degree of either renal or hepatic functional impairment.
- Intra-abdominal pressure if significantly increased, it will impair both portal and renal blood flow.
Kidney & Excretion Problem

- The parent drug and metabolites may accumulate in RF.
- Morphine is metabolized to morphine-3-glucuronide and morphine-6-glucuronide. Morphine-6-glucuronide is an active metabolite eliminated by the kidneys.
- In renal failure, morphine-6-glucuronide may accumulate, and it has been associated with toxicity.
- Normeperidine may accumulate and cause central nervous system (CNS) excitability and possible seizures.
Principles of Sedation

- Safety
- Minimal physical discomfort and pain
- Minimal psychological trauma
- Amnesia
- Behavior control/ immobility
- Rapid return to a state of alertness
Ideal PICU Sedative/Analgesic

- Rapid onset and Rapid recovery
- Predictable duration
- No active metabolites
- Multiple routes of delivery
- Easy to titrate
- Minimal cardiopulmonary effects
- Not altered by renal or hepatic disease
- No drug interactions
- Wide therapeutic index
COMMON DRUGS UTILIZED

- Opiates (Narcotics)
- Benzodiazepines
- Chloral hydrate
- Barbiturates
- Ketamine
- Propofol
- Neuroleptics
- Paralytics?!
Define The Goals

- Is the patient in pain?
- Is the child anxious?
- Does the case require immobility?
- Does the child need to be interactive?
- Will the effects of administered drugs interfere with the patient exam?
Common Conditions in PICU

- MECHANICAL VENTILATION
  - Respiratory failure
  - Airway
  - Neurological
- POST-OPERATIVE
- HEAD INJURY
- PULMONARY HYPERTENSION
- PROCEDURES
Choosing the Right Drug

Sedation
- Amnesia
- Hypnosis
- Anxiolysis

Analgesia

Benzodiazepines

\(\alpha\)-2 agonists (Dexmedetomidine)

Opioids
## Analgesics inappropriate for use in the ICU

<table>
<thead>
<tr>
<th>Drug</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Meperidine</td>
<td>Analgesia not superior to morphine; normeperidine metabolite is renally eliminated and has neurotoxic effects, including seizures and delirium.</td>
</tr>
<tr>
<td>Codeine</td>
<td>Low analgesic potency when administered parenterally; most of its analgesic effect is due to hepatic metabolism to morphine.</td>
</tr>
<tr>
<td>Methadone</td>
<td>Extended duration of activity increases risk of accumulation and adverse effects with repeated dosing.</td>
</tr>
<tr>
<td>Nonsteroidal antiinflammatory drugs (NSAIDs)</td>
<td>Analgesia not superior to opiates; platelet inhibition, antiprostaglandin effects increase risk of stress ulcers and renal injury.</td>
</tr>
</tbody>
</table>
# Alternative sedative agents in the PICU

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose (mg/kg)</th>
<th>Route</th>
<th>Interval (hrs)</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diphenhydramine</td>
<td>0.5–1</td>
<td>PO, IV, IM</td>
<td>4–6</td>
<td>Antihistamine; provides sedation and is antipruritic and antiemetic&lt;br&gt;Adverse effects include dry mouth, tachycardia, and respiratory depression</td>
</tr>
<tr>
<td>Promethazine</td>
<td>0.5–1</td>
<td>IV, PO, PR, IM</td>
<td>6–8</td>
<td>Phenothiazine commonly used as an antiemetic&lt;br&gt;Risk of causing extrapyramidal reactions and neuroleptic malignant syndrome</td>
</tr>
<tr>
<td>Haloperidol</td>
<td>0.01–0.02</td>
<td>IV, IM</td>
<td>8–12</td>
<td>Antipsychotic; can have dystonic reactions and neuroleptic malignant syndrome</td>
</tr>
<tr>
<td></td>
<td>0.1–0.2</td>
<td>PO</td>
<td>Not for p.r.n. use</td>
<td></td>
</tr>
<tr>
<td>Chlороral hydrate</td>
<td>50–100</td>
<td>PO, PR</td>
<td>24</td>
<td>Aliphatic alcohol, unknown mechanism of action&lt;br&gt;Not to be used repetitively or in prolonged fashion&lt;br&gt;Unpredictable onset and duration of sedative effects&lt;br&gt;GI irritant&lt;br&gt;No analgesic effects</td>
</tr>
<tr>
<td>Clonidine</td>
<td>0.002–0.005</td>
<td>PO</td>
<td>4–6</td>
<td>α2 adrenergic agonist&lt;br&gt;Possible hypotension&lt;br&gt;Potentiates sedative/analgesic effects of other agents&lt;br&gt;Available in transcutaneous patches of 0.1, 0.2, 0.3 mg, which are changed every 7 days</td>
</tr>
</tbody>
</table>
Consensus guidelines on sedation and analgesia in critically ill children

Paediatric Intensive Care Society Sedation, Analgesia and Neuromuscular Blockade Working Group


Stephen Playfor Ian Jenkins
Carolyne Boyles ImtiChoonara
Gerald Davies Tim Haywood
Gillian Hinson Anton Mayer
Neil Morton Tanya Ralph
Andrew Wolf
Recommendations

1. Non-pharmacological interventions
2. Pain assessment and analgesic management
3. Sedation assessment and sedative agents commonly used in the PICU
4. Withdrawal syndrome assessment, prevention and management
Non-pharmacological interventions: environmental factors, relaxation, distraction, promotion of sleep and day–night orientation

**Recommendations:**
- Any correctable environmental and physical factors causing discomfort should be addressed alongside the introduction of pharmacological agents.
- A normal pattern of sleep should be encouraged.
- Attention should be paid to lighting, environmental noise and temporal orientation of patients.
Pain assessment and analgesic management

Recommendations:

- All critically ill children have the right to adequate relief of their pain.
- Local and regional anaesthetic techniques should be considered.
- A patient controlled analgesia (PCA) device may be useful in older children.
Pain assessment

Recommendations

- Pain assessment should be performed regularly by using a scale appropriate to the age of the patient and routinely documented.
- The level of pain reported by the patient must be considered the current standard of analgesia.
- Patients who cannot communicate should be assessed for the presence of pain-related behaviours and physiological indicators of pain.
- A therapeutic plan for analgesia should be established for each patient and regularly reviewed.
Recommended analgesic agents

Recommendations

- Continuous intravenous infusions of morphine or fentanyl are recommended for the relief of severe pain.

- Non-steroidal anti-inflammatory drugs? or paracetamol may be used as adjuncts to opioids in certain patients.
Sedation assessment and sedative agents commonly used in the PICU

**Recommendations**

- Adequate analgesia should be provided to all critically ill children regardless of the need for sedation.
- The level of sedation should be regularly assessed and documented using a sedation assessment scale, wherever possible using a validated scoring system such as the **COMFORT** scale.
- The desired level of sedation should be identified for each patient and should be regularly reassessed.
- Doses of sedative agents should be titrated to produce the desired level of sedation.
Recommended and commonly used sedative agents in PICU

**Recommendation**

- **Midazolam** is the recommended agent for the majority of critically ill children requiring intravenous sedation. It should be given by **continuous infusion**.

- Early use of enteral sedative agents is recommended.

- **Propofol** should not be used to provide continuous sedation in critically ill children.
Withdrawal syndrome assessment, prevention and management

Recommendation

- The potential for opioid and benzodiazepine withdrawal syndrome should be considered after 7 days of continuous therapy.

- When subsequently discontinued, the doses of these agents may need to be routinely tapered.
Conclusions

• The quality of evidence available in the literature to support these recommendations is poor.

• There is little evidence to guide PICU staff with the common clinical problems of tolerance, withdrawal, and the patient who requires long-term sedation, or who is difficult to sedate appropriately with standard agents.
Key Points
Definitions confused with addiction

- **Drug tolerance:** need for larger dose of opioid to maintain original effect.

- **Physical dependence:** withdrawal symptoms when chronic use of opioid is discontinued or opioid antagonist (Narcan) is given.
Narcotic Addiction

Behavioral and voluntary pattern
- characterized by compulsive drug-seeking behavior
- leading to overwhelming involvement with procurement, and
- use of opioid NOT for medical reasons, such as pain relief.
Key Points

- The treatment and alleviation of pain is a basic human right for everyone, regardless of age.
- Pain is a subjective experience.
- Pain and sedation assessment and management are interdependent, and one is essentially useless without the other.
pharmacokinetic & pharmacodynamic

- Sedatives and analgesics are given by titration to effect.

- Many PICU patients require enormous doses of analgesics and sedatives, doses so high, that to an outsider they seem preposterous if not dangerous.
Mild Analgesia

- The most commonly used nonopioid analgesic in pediatric practice remains acetaminophen (paracetamol).

- Avoid NSAID if possible: platelet inhibition, risk of stress ulcers and renal injury.
Strong Analgesia

- The opioids most commonly used in the management of pain are µ agonists.
- These include morphine, meperidine, methadone, codeine, and the fentanyl.
- At equianalgesic doses, the pharmacodynamic effects of all of the µ-opioid agonists are similar and include:
  - Analgesia & Sedation
  - Respiratory depression
  - Nausea and vomiting & Constipation
  - Pruritus. Miosis
  - Tolerance, and physical dependence.
Opioids in PICU

- **Fentanyl** is 50 to 100 times more potent than morphine. and
- Fentanyl has become the most commonly used analgesic for procedures and pain control in the PICU.
- It is short-acting following single doses (redistribution) but long-acting following infusions.
- Methadone can be used to wean patients following prolonged analgesic therapy.
Multifactorial Effects

Anxiety, fear, a sense of helplessness, and lack of sleep will potentiate pain and, if left untreated, can lead to psychosis in critically ill patients.
Sedation ≠ Analgesia

- Most sedatives, such as:
  - The benzodiazepines
  - Chloral hydrate
  - The barbiturates, and
  - All neuromuscular blocking agents

have no analgesic properties and may actually exacerbate pain.
Benzodiazepines

- The benzodiazepines are extremely potent:
  - amnestics,
  - anticonvulsants,
  - sedatives,
  - hypnotics,
  - skeletal muscle relaxants,
  - effective whether given parenterally or enterally, and produce dose-dependent depression of breathing.

- Benzodiazepine-withdrawal symptoms are well described (Like opiates)
Anesthesia in PICU

- Unexpected fatal lactic acidosis in critically ill children who are sedated for prolonged periods with propofol (propofol infusion syndrome) precludes prolonged (>6 hrs) use in the PICU.
- The use of inhalational anesthetic agents (N2O, isoflurane) in the PICU is limited by institutional and nursing credentialing, availability of specialized delivery and monitoring equipment, and the ability to scavenge exhaled gas.
Dexmedetomidine

α2 Agonists, particularly dexmedetomidine, are a new tool in the sedation of ventilated and nonventilated patients in the PICU
Withdrawal Risk

- When physical dependence has been established, sudden discontinuation of an opioid or benzodiazepine agonist produces a withdrawal syndrome within 24 to 72 hrs of drug cessation.
- A simplified, weaning protocol with close observation is recommended to assess withdrawal symptoms and guide therapy.
Thank You