Prevention and treatment of pain in hospitalized infants, children, and teenagers: from myths and morphine to multimodal analgesia

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Learning Objectives

• Critically review risks and safety of analgesic under-treatment versus over-treatment in hospitalized infants and children with pain

• Evaluate assumptions about opioid use in children

• Discuss how multiple agents, interventions, rehabilitation, psychological and integrative (“non-pharmacologic”) therapies act synergistically for more effective pediatric pain control with fewer side effects than a single analgesic or modality

5-year old Marius:
Procedural Pain Management

Don't have enough staff for pediatric pain control...?

Funny, how there is always enough staff to restrain a child.

Pediatric Analgesia in 1985
“Papoose Boards”

So, how do we treat the individual pain patient in front of us?

Spoiler Alert: Crystal-clear answer on 3rd last slide!
Pediatric Pain - Status Quo

• Under treatment of pain in children

• Parents expect pain to be relieved

• Priorities of parents of hospitalized children: "Taking care of pain" rated as second highest priority (1st: getting right diagnosis)

• Parents’ greatest distress: failing to protect their child from pain

• USA: adults receive more than two to three times as many analgesic doses as children (with identical diagnoses)

• The younger children are, the less likely they receive appropriate analgesia

• NICU: increased morbidity & mortality

Inappropriate Analgesia: Why Bother...?

• Children with persistent pain suffer more physical symptoms in adult life, more anxiety and more depression

• Pain ratings at 4-6 months routine vaccination higher for circumcised versus uncircumcised boys

• Up to 25% of adults have fear of needles with most fears developing in childhood: avoidance of health care (including non-adherence with vaccination schedules)

• NICU: increased morbidity & mortality
Trauma & post-traumatic stress disorder (PTSD)

- **Children (n=48) with injury** that led to hospital treatment: Morphine was associated with lower levels of PTSD at follow-up 6 months later. Nixon RD, Nehmy TJ, Ellis AA, Ball SA, Menne A, McKinnon AC. Predictors of posttraumatic stress in children following injury: The influence of appraisals, heart rate, and morphine use. Behaviour research and therapy. 2010 Aug;48(8):810-5.


Myths and Barriers to Using Opioids

**Case Scenario:**

- You are taking care of a child with severe acute somatic nociceptive pain following major trauma. It crosses your mind to administer a strong opioid such as morphine, fentanyl, or hydromorphone.

- What would be the most common concerns you might hear from your colleagues or parents arguing against opioid use in this child?

Common Opioid Assumptions

**Addiction** - a chronic relapsing condition characterized by persistent, compulsive dependence on a behavior or substance despite adverse consequences.

- Tolerance ≠ addiction
- Pseudo-addiction

**Masking symptoms**

- Abdominal Pain
- Over Sedation / Respiratory Depression
- Ileus / Constipation
- Medication “Too strong”
How Do We Manage Acute Pain in Children?

WHO guidelines on the pharmacological treatment of persisting pain in children with medical illnesses (2012)

- Dosing at regular intervals (“By the Clock”)
- Adapting treatment to the individual child (“With the Child”)
- Using the appropriate route of administration (“By the appropriate route”)
- Using a two-step strategy (“By the Analgesic Ladder”)
WHO Principle 1: Dosing at Regular Intervals

- PRN ("as needed")
- **PRN = Patient Receives Nothing**
- When pain is constantly present, analgesics should be administered, while monitoring side-effects, at regular intervals
- "By the clock" and NOT as an "as needed" (or pro re nata "PRN") basis
- Regular scheduling ensures a steady blood level, reducing the peaks and troughs of PRN ("as needed") dosing
- PRN (as needed) only:
  - May take several hours & higher opioid doses to relieve pain
  - Results in cycle of undermedication and pain, alternating with periods of overmedication and drug toxicity


WHO Principle 2: Adapting Treatment to the Individual Child

- Treatment should be tailored to the individual child and opioid analgesics should be titrated on an individual basis
- At analgesic dosing: no sedation expected
  - The effective dose is what relieves the pain
  - Different children may respond differently to same dose
  - Effective dose must be adjusted to child's needs
  - Dose of strong opioids: only the sky is the limit
- Assess response frequently
  - Pain Scales
  - Look for opioid-induced side effects and toxicity

Regular (!) Pain Assessment

- One-dimensional self-report scores
- Multi-dimensional rating scores

Infant FLACC Scale

<table>
<thead>
<tr>
<th>Item</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Facial expression</td>
<td>0-3</td>
</tr>
<tr>
<td>Leg movement</td>
<td>0-3</td>
</tr>
<tr>
<td>Arm movement</td>
<td>0-3</td>
</tr>
<tr>
<td>Cry/consolation</td>
<td>0-3</td>
</tr>
<tr>
<td>Activity level</td>
<td>0-3</td>
</tr>
</tbody>
</table>

Children who are uncooperative or who are unable to communicate may be assessed with a close observer rating or cooperative rating. A single rating may be used for non-compliant or cooperation in the naive observer.
What are we measuring...

(1) **Nociceptive Pain:**
arises from the activation of peripheral nerve endings (nociceptors) that respond to noxious stimulation
- **Somatic** (for example, muscles, joints)
- **Chronic somatic** pain typically well localized & often results from degenerative processes (such as arthritis)
- **Visceral** (internal organs)

(2) **Neuropathic Pain:**
resulting from injury to, or dysfunction of, the somatosensory system.
- **Central pain:** caused by a lesion or disease of the central somatosensory nervous system

(3) **Psycho-social-spiritual-emotional Pain / Total Pain**

(4) **Chronic Pain**
- Pain beyond expected time of healing

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Measuring pain alone...

High specificity, low sensitivity...? Don't forget:

- **Withdrawal:** WAT-1 score

- **Delirium:** CAPD

- **Sedation:** SBS score
Route of Administration

WHO guidelines on the pharmacological treatment of persisting pain in children with medical illnesses (2012)

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- **Using a two-step strategy ("By the Analgesic Ladder")**

**WHO Principle 4: Using a Two-Step Strategy**

**WHO Step 1**
Mild Pain

**Ibuprofen**
and/or
**Acetaminophen** (Paracetamol)

Other NSAIDs?
Cox-2 Inhibitor?
**Nociceptive Pathways & Primary Sites of Action of Analgesics**

Injury → Thalamus

**Citius, Altius, Fortius...?**

- Ibuprofen salts: fast-acting formulations
- Advil® Film-Coated Tablets, contains 266 mg of ibuprofen sodium (equivalent to 200 mg of standard ibuprofen)
- Produced significantly **better analgesia over 6h**, fewer re-medication than standard formulations
- 200-mg fast-acting ibuprofen (NNT 2.1; 95% confidence interval 1.9-2.4) was as effective as 400 mg standard ibuprofen (NNT 2.4; 95% CI 2.2-2.5), with faster onset of analgesia.

- More rapid absorption, faster initial pain reduction, good overall analgesia in more patients at the same dose, and probably longer-lasting analgesia, but with no higher rate of patients reporting adverse events.

- However, earlier onset preferred in other pain condition, such as chronic nociceptive or neuropathic pain?

**WHO Principle 4: Using a Two-Step Strategy**

**WHO Step 1**
- Mild Pain
  - Ibuprofen
  - and/or Acetaminophen (Paracetamol)
  - Other NSAIDs? Cox-2 Inhibitor?

**Intermediate Step**
- Tramadol
- Codeine
- Hydrocodone
WHO Principle 4: Using a Two-Step Strategy

**WHO Step 1**
Mild Pain
- Ibuprofen
- and/or Acetaminophen (Paracetamol)
- Other NSAIDs? Cox-2 Inhibitor?

**WHO Step 2**
Moderate to Severe Pain
- Morphine
  - or fentanyl, hydromorphone, oxycodone, methadone (UK: diamorphine)

Nociceptive Pathways & Primary Sites of Action of Analgesics

**Opioids**
- Pre-synaptic nerve terminal
  - Neurotransmitter release
- Post-synaptic nerve terminal
  - Membrane hyperpolarization
=> suppress neuronal excitability

**NSAIDs**

**Acetaminophen** (Paracetamol)

**Injury**

**Thalamus**
Integrative Pain Management

State of the art pain management in the 21st century demands that pharmacological management must be combined with supportive and integrative, non-pharmacological therapies to manage a child's pain.

- **Physical methods** (e.g. cuddle/hug, massage, comfort positioning, heat, cold, TENS)
- **Cognitive behavioral techniques** (e.g. guided imagery, hypnosis, abdominal breathing, distraction, biofeedback)

Integrative Pain & Symptom Management

A Pediatrician’s Top 10 Apps for Distraction & Pain Management [http://NoNeedlessPain.org](http://NoNeedlessPain.org)
6-year-old Cassandra with severe pain due to chest tube insertion
Fentanyl PCA “the pump” and blowing bubbles “going to bubble land”

How does this stuff work...?


- Distraction significantly increased activation of cingulo-frontal cortex including orbitofrontal & perigenual anterior cingulate cortex (ACC), as well as periaqueductal gray (PAG) & the posterior thalamus.

Regional anesthesia approaches to pain management in PC

- **Regional anesthesia:** pediatric knowledge limited to case reports and case series.
  - central neuraxial infusions
  - peripheral nerve and plexus blocks or infusions
  - neurolytic blocks
  - implanted intrathecal ports & pumps for baclofen, opioids, local anesthetics, and other adjuvants

- **Neurolytic Sympathectomy:**
  - RCT (n=109) inoperable abdominal or pelvic cancer: better pain control, less opioid consumption, and better quality of life

Non-Opioids
- Acetaminophen / Paracetamol
- NSAIDs

Regional Anesthesia
- Neuraxial infusion
- Peripheral/Plexus Nerve block
- Neurolytic block
- Intrathecal port/pump
- Intraventricular opioids?
- Percutaneous cervical cordotomy?

Opioids
- Tramadol (weak)
- Morphine (strong)

4 WHO-Principles
- "By the clock"

Integrative Therapies
- Such as:
  - Massage
  - Distraction
  - Deep Breathing
  - Biofeedback
  - Aromatherapy
  - Hypnosis

Psychology
- CBT

Rehabilitation
- Exercise
- Physical Therapy
- Sleep Hygiene
- Occupational Therapy
- Child Life

Adjuvants
- Such as:
  - Alpha-Agonist
  - Gabapentinoids
  - TCA/Antidepressants
  - NMDA-Antagonists
  - Na-channel blockers

Multimodal (Opioid-sparing) Analgesia

- Acute
- Chronic
- 4 WHO-Principles
- "By the clock"
Multimodal Analgesia

- Multimodal (opioid-sparing) analgesia: Multiple agents, interventions, rehabilitation, psychological and integrative therapies act synergistically for more effective pediatric pain control with fewer side effects than single analgesic or modality

Multimodal = Awesome!


- (Adults): Multimodal analgesia therapy (versus PCA only) reduces length of hospitalization in patients undergoing surgery


What’s Plan B?

If adequate procedural analgesia not feasible with the “4 Non-Negotiables” alone, refer patient to:

1. Child Life (should’ve been involved by now!)

2. Needle Phobia: psychology (CBT)

3. Mild sedation: Nitrous gas


4. Moderate/deep sedation (e.g. ketamine, propofol)

Note:
A sedative alone (such as a benzodiazepine) can never be a substitute for procedural analgesia.
IV Access Under Nitrous Gas

22 months-old, Lidocaine 4% cream in place, needed IV for radiologic procedure, history of challenging IV access in the past

Thanks to Patricia D. Scherrer MD, Medical Director, Sedation Services
Children’s Hospitals and Clinics of Minnesota

Do you remember Marius...?

How about a Plan B!

LET Anesthesia

- Sitting upright
- Distraction
- Topical Anesthesia

- 3mL LET-gel: Lidocaine 4%-Epinephrine 0.18% - Tetracaine 0.5%

So, how do we treat the individual pain patient in front of us?

Crystal clear answer:

“It Depends”
-Socrates

Conclusions

- Withholding evidence-based analgesia to hospitalized infants/children in pain not only unethical, but causes immediate and long-term harm.
- Potential risks in safety of analgesics are real, but manageable; cannot justify denying administration of pain medications to pediatric patients.
- Use multimodal (opioid-sparing) analgesia: Multiple agents, interventions, rehabilitation, psychological and integrative therapies act synergistically for more effective pediatric pain control with fewer side effects than single analgesic or modality.
Further Training

**10th Annual Pediatric Pain Master Class**
- Minneapolis, Minnesota, USA | June 17-23, 2017 [http://tinyurl.com/PedsPMC](http://tinyurl.com/PedsPMC)

**Education in Palliative & End-of-life Care (EPEC): Become an EPEC-Pediatrics Trainer**
- Montréal, Quebec, Canada | April 28-30, 2017 (Professional Development Workshop 04/28/17) [http://tinyurl.com/EPECpeds](http://tinyurl.com/EPECpeds)

**11th International Symposium on Pediatric Pain (ISPP)**

Contact: CIPPC@ChildrensMN.org

Blog: [http://NoNeedlessPain.org](http://NoNeedlessPain.org)