New Strategies for Prevention and Treatment of Pain in Pediatric Trauma Patients

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Greetings from Minneapolis

Learning Objectives

• Critically review risks and safety of analgesic under-treatment versus over-treatment in hospitalized infants and children with trauma pain
• Evaluate differences in treatment approach for acute, procedural, neuropathic, psycho-social, and/or chronic-persistent pain
• Discuss how multiple agents, interventions, rehabilitation, psychological and integrative (“non-pharmacological”) 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


Pediatric Analgesia in 1985
“Papoose Boards”

4 Sizes to Fit All Ages

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

Funny, how there is always enough staff to restrain a child.
What are children most afraid of when coming to see a doctor?


Pain Pathophysiology
Pediatric Trauma Patients

(1) Nociceptive Pain: arises from the activation of peripheral nerve endings (nociceptors) that respond to noxious stimulation [e.g. localized, sharp, squeezing, stabbing, or throbbing]

- Tissue damage / trauma
- Post-surgical pain
- Procedural Pain: Dressing changes, intravenous access, injections

(2) Neuropathic Pain: resulting from injury to, or dysfunction of, the somatosensory system. [burning, shooting, electric, or tingling]

  - n=358; burns covering an average of 59% of their bodies
  - 12 years later: 52% of respondents reported ongoing burn-related pain

(3) Visceral (internal organs) [poorly localized, dull, crampy, or achy]

(4) Psycho-social-spiritual-emotional Pain / Total Pain

(5) Persistent (Chronic) Pain

- Chronic post surgical pain (CPSP)
  - n=358; burns covering an average of 59% of their bodies

- Pain beyond expected time of healing

A feasibility study showing cortical plasticity in chronic neuropathic pain following burn injury.
So, how do we treat the individual pain patient in front of us?

Hmhh... 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
- Assumption: everything possible is done

Pediatric Pain - Status Quo

- USA: adults receive more than two - three times as many analgesic doses as children (with identical diagnoses)
- Compared to adults, pediatric patients receive fewer and/or incorrectly dosed analgesics in daily routine
- The younger children are, the less likely they receive appropriate analgesia

Parents' influence on pain treatment in children
- Parents' expectations play a role in the management of pain in children
- Communication between parents and healthcare providers is crucial for effective pain management

Comparison of analgesic dosing in children and adults
- Children receive fewer analgesic doses compared to adults
- More frequent and higher dosing in adults
- Importance of individual patient assessment

References:
Inappropriate Analgesia: Why Bother...

- Children with persistent pain suffer more physical symptoms in adult life, more anxiety and more depression. (1946 Medical Research Council and 1958 National Child Development Study)
- Pain ratings at 4-6 months routine vaccination higher for circumcised versus uncircumcised boys. (Taddio A, Katz J, Ilersich AL, Koren G. Effect of neonatal circumcision on pain response during subsequent routine vaccination. Lancet. 1997;349(9052):599-603.)

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.)

How Do We Manage Acute Pain in Children?
No Needless Pain
Multimodal Analgesia

Multimodal (Opioid-sparing) Analgesia

Basic Analgesics
- Acetaminophen / Paracetamol
- NSAIDs

Nociceptive Pathways & Primary Sites of Action of Analgesics

Injury
Acetaminophen (Paracetamol)
NSAIDs
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-medications 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? Peloso, P. M., Faster, higher, stronger: to the gold medal podium? Pain, 2014. 155(1): p. 4-5.

Multimodal (Opioid-sparing) Analgesia

- Basic Analgesics
  - Acetaminophen / Paracetamol
  - NSAIDs

- Opioids
  - Tramadol ("weak")
  - Morphine ("strong")

4 WHO-Principles
- "By the clock"
- PRN ("as needed")
- PRN = Patient Receives Nothing

- When pain is constantly present, analgesics should be administered, while monitoring side-effects, at regular intervals
- At analgesic dosing: no sedation expected

Nociceptive Pathways & Primary Sites of Action of Analgesics

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

Acetaminophen (Paracetamol)
Measuring pain alone…?

High specificity, low sensitivity…? Don’t forget:

- **Withdrawal**: WAT-1 score
- **Delirium**: CAPD
- **Sedation**: SBS score

*Dr. Cox, should I ever use Codeine or Hydrocodone (Vicodine) in my trauma patients?*
Cytochrome P450 2D6

Inactive Prodrug: Codeine
Active Metabolite: Morphine

Inactive Prodrug: Hydrocodone
Active Metabolite: Hydromorphone (Dilaudid®)

Inactive Prodrug*: Hydrocodone
Active Metabolite: Hydromorphone (Dilaudid®)

Current body of evidence cannot support whether the main analgesic effect results from hydrocodone or the metabolite hydromorphone


FDA Tramadol Announcement

04/20/2017

- FDA's strongest warning, called a Contraindication, to the drug labels of codeine and tramadol stating that codeine should not be used to treat pain or cough and tramadol should not be used to treat pain in children younger than 12 years.
- A new Contraindication to the tramadol label warning against its use in children younger than 16 years to treat pain after surgery to remove the tonsils and/or adenoids.

https://www.fda.gov/Drugs/DrugSafety/ucm549679.htm

Slow metabolizers: Parent compound (Tramadol) remains active, hence only diminished effect on analgesia

Tramadol

Compounding Formula for 5mg/mL oral suspension:

<table>
<thead>
<tr>
<th>Ingredient</th>
<th>Quantity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tramadol</td>
<td>50 mg Tabs #12</td>
</tr>
<tr>
<td>Ora-Plus</td>
<td>60 ml</td>
</tr>
<tr>
<td>Ora-Sweet</td>
<td>QSAD® 120 ml</td>
</tr>
</tbody>
</table>

*Add Quantity Sufficient to Make (total)*

Shake well & must be refrigerated. 90 day exp. date

**Pediatric Dose Suggestion**

- 1-2 mg/kg Q3-6 h PO [max 8 mg/kg/day] (if < 50 kg)
- 50-100 mg Q3-6 h PO [max 400 mg/day] (if > 50kg)
- e.g. 50 mg Q6h plus 50 mg Q3h PRN

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**Which Opioid to choose?**

**Recommended**
- Tramadol
- Morphine
- Fentanyl
- Oxycodone
- Hydromorphone
- Methadone

**NOT Recommended**
- Codeine
- Hydrocodone/Acetaminophen (e.g., Vicodin®)
- Oxymorphone
- Oxycodone/Acetaminophen (e.g., Percocet®)

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**Multimodal (Opioid-sparing) Analgesia**

**Non-Opioids**
- Acetaminophen
- Paracetamol
- NSAIDs

**Opioids**
- Tramadol ("weak")
- Morphine ("strong")

**4 WHO-Principles**
- "By the clock"
- "Integrative Therapies"
  - Such as: Massage, Distraction, Deep Breathing, Biofeedback, Aromatherapy, Hypnosis

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Integrative modalities

- **Integrative modalities effective in management of pediatric pain**
  

- **Hypnosis**
  

- **Guided imagery**
  
  Dobson, C.E.; Byrne, M.W. Original research: Using guided imagery to manage pain in young children with sickle cell disease. The American journal of nursing 2014, 114, 26-36; test 37, 47.

- **Yoga**
  

- **Acupuncture**
  

- **Massage**
  

- **Biofeedback**
  

Integrative Pain & Symptom Management

A Pediatrician’s Top 10 Apps for Distraction & Pain Management [http://NoNeedlessPain.org](http://NoNeedlessPain.org)

- Balloonimals Games
- Biodeck Healthcare & Fitness
- Healing Buddies Comfort Kit
- Naturespace: Relax Entertainment
- Sand Garden Entertainment
- Simply Being - Qui... Healthcare & Fitness

6-year-old Cassandra with severe pain due to chest tube insertion

Fentanyl PCA “the pump” and blowing bubbles “going to bubble land”
Nociceptive Pathways & Primary Sites of Action of Analgesics

Thalamus

Periaqueductal grey (endorphins)

Integrative (non-pharmacological) therapies

Opioids

NSAIDs

Acetaminophen (Paracetamol)

NSAIDs

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.

Graded Motor Imagery

- Process of thinking about moving without actually moving.

- Gray Matter: Cortical reorganization and associated changes in somatosensory cortex activity and anatomy in certain types of pain.

  - Degree of cortical reorganization correlated with pain intensity.

Mirror Visual Feedback

Non-Opioids

- Acetaminophen / Paracetamol
- NSAIDs

Integrative Therapies

- Massage
- Distraction
- Deep Breathing
- Biofeedback
- Aromatherapy
- Hypnosis

Opioids

- Tramadol (“weak”)
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4 WHO-Principles

- “By the clock”

Regional Anesthesia

- Neuraxial infusion
- Peripheral/Plexus Nerve block
- Neurolytic block
- Intrathecal port/pump
- Intraventricular opioids?
- Percutaneous cervical cordotomy?
Regional anesthesia approaches to pain management in PC

- **Regional anesthesia:**
  - 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**

- Opioids
  - **Tramadol (weak)**
  - **Morphine (strong)**

- Multimodal (Opioid-sparing) Analgesia
  - **Regional Anesthesia**
    - **Neuraxial infusion**
    - **Peripheral/Plexus Nerve block**
    - **Neurolytic block**
    - **Intrathecal port/pump**
    - **Intraventricular opioids?**
    - **Percutaneous cervical cordotomy?**

- Integrative Therapies
  - **Massage**
  - **Distraction**
  - **Deep Breathing**
  - **Biofeedback**
  - **Aromatherapy**
  - **Hypnosis**

- Psychology
  - **CBT**

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

- Adjuvants
  - **Alpha-Agonist**
  - **Gabapentinoids**
  - **TCA/Antidepressants**
  - **NMDA-Antagonists**
  - **Na-channel blockers**
  - Antiglucocorticoids
  - Corticosynthetic
  - Mucho relaxants
  - Antidepressants/corticosteroids
  - Bisphosphonates

- Transition from acute to chronic pain

- **Chronic post surgical pain (CPSP) after Surgery:** last at least 2 months, other causes were excluded
- **18% of children developed CPSP; associated with parental catastrophizing:**

- **CBT**

- **Exercise**

- **Physical Therapy**

- **Sleep Hygiene**

- **Occupational Therapy**

- **Child Life**

- **Antiglucocorticoids**

- **Corticosynthetic**

- **Mucho relaxants**

- **Antidepressants/corticosteroids**

- **Bisphosphonates**
Chronic Pain in Children

- Pain lasting > 3-6 months: Time definition arbitrary
- Pain that extends beyond the expected period of healing
- Hence lacks the acute warning function of physiological nociception


Chronic-on-acute Pain

- Approximately 5% of children and teenagers in general population have significant pain related dysfunction
  - In USA: > 3.7 million children
- At least (!) 5% of children with sickle cell disease, inflammatory bowel disease, rheumatoid arthritis, congenital heart disease, or cancer are expected to display chronic pain in addition to their underlying somatic pain episode

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!

2016 Guidelines on the Management of Postoperative Pain


- (Adults): Multimodal analgesia therapy (versus PCA only) reduces length of hospitalization in patients undergoing surgery
4 steps to make needles less painful

1. Numb the skin
2. Sugar water or breastfeeding for babies
3. Comfort positioning
4. Distraction

Watch videos at childrensmn.org/comfortpromise.

Needle pokes without the pain?

J-Tip in the Emergency Room (CBS 4 Morning News)

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%


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

1. Child Life (shouldn’t have been involved by now?)
2. Needle Phobia: psychology (CBT)
3. Mild sedation: Nitrous gas
   - or
3. 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.
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 Links

- Video: Kiran Stordalen and Horst Rechelbacher Pediatric Pain, Palliative and Integrative Medicine Clinic Tour [https://vimeo.com/12264981]
- Short Movie Meet the Interdisciplinary Chronic Pain Clinic Team at Children’s Minnesota LittleStars TV [https://vimeo.com/133313795]
- Video: Tour of the Kiran Stordalen and Horst Rechelbacher Pediatric Pain, Palliative and Integrative Medicine Clinic at Children’s Hospitals and Clinics of Minnesota and an overview of the three programs that are offered at Children’s under this clinic. [https://vimeo.com/133313795]
- Short Movie LittleStarsFilm ‘Kali’s Story - Beyond the NICU’/This amazing pediatric palliative care short movie (7 min) features 8-year-old Kali’s journey at Children’s Hospitals and Clinics of Minnesota from NICU to today, receiving care by the Pain & Palliative & Integrative Medicine program while inpatient, in the clinic, and at home (Jan 22, 2015) [http://www.littlestars.tv/short-film/beyond-the-nicu]

Further Training
Contact: CIPPC@ChildrensMN.org

11th Annual Pediatric Pain Master Class
- Minneapolis, Minnesota, USA | June 9-15, 2018 [http://tinyurl.com/PedsPMC]

Education in Palliative & End-of-life Care [EPEC]: Become an EPEC-Pediatrics Trainer
- September 2018 [http://tinyurl.com/EPECPeds]

12th International Symposium on Pediatric Pain (ISPP)

Thank You