Prevention and Treatment of Pain in Pediatric Trauma Patients.

Stefan J. Friedrichsdorf, MD, FAAP
Medical Director, Department of Pain Medicine, Palliative Care & Integrative Medicine
Children’s Hospitals and Clinics of Minnesota, Minneapolis/St. Paul, MN

Associate Professor of Pediatrics, University of Minnesota Medical School

stefan.friedrichsdorf@childrensMN.org  Twitter: @NoNeedlessPain

Learning Objectives

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

Pain after trauma injury: Multifactorial

- Acute pain
  - Tissue damage, repetitive trauma
- Procedural pain
  - Dressing changes, intravenous access
- Neuropathic pain
- Psycho-spiritual-spiritual pain
- Chronic pain
- Chronic post surgical pain
- Pain can persist after healing
  - n=358 burns covering an average of 39% of their bodies
  - 12 years later: 52% of respondents reported ongoing burn-related pain
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.
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, Ilerich 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)

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** — “chronic relapsing condition characterized by persistent, compulsive dependence on a behavior or substance despite adverse consequences”
- Tolerance ≠ addiction
- Pseudo-addiction
- **Over Sedation / Respiratory Depression**
- **Ileus / Constipation**
- Medication “Too strong”

Masking symptoms

- Abdominal Pain
- Opioids after major cranial surgery in children do NOT result in altered mental status nor respiratory depression
- As always... Think first! (e.g. compartment syndrome?)... analgesia second...

How Do We Manage Acute Pain in Children?

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

---

Pain in children with impaired communication

- **Non-communicating Children’s Pain Checklist - Revised (NCCPC-R); postoperative Version (NCCPC-PV)**
- **Pediatric Pain Profile (PPP)**
- **r-FLACC**

---

Measuring pain alone...

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

- **Withdrawal:** WAT-1 score
- **Delirium:** CAPD
- **Sedation:** SBS score
Route of Administration

Analgesic Medications

- Oral
- Intravenous / Subcutaneous
- Intranasal (MAD device)
- Nebulization
- Sublingual
- Transmucosal
- Transdermal
- Suppository

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
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.

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

Injury

Acetaminophen
- Paracetamol
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

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 [link]
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

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


- **central neuraxial infusions**
- **peripheral nerve and plexus blocks or infusions**
- **neurolytic blocks**
- Implanted intrathecal ports & pumps for baclofen, opioids, local anesthetics, and other adjuvants

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

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

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

4 WHO-Principles
- "By the clock"

**Regional Anesthesia**
- Neuraxial infusion
- Peripheral/Plexus Nerve block
- Neurolytic block
- Intrathecal port/pump
- Intraventricular opioids

**Adjuvants**
- Alpha-Agonist
- Gabapentinoids
- TCA/Antidepressants
- NMDA-Antagonists
- Na-channel blockers
- Antidepressants
- Benzodiazepines
- Carbamazepine
- Muscle relaxants
- Radionuclides
- Bisphosphonates

**Psychology**
- CBT

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

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

**Non-Opioids**

**Integrative Therapies**

**Regional Anesthesia**

**Adjuvants**

**Psychology**

**Rehabilitation**

**Nociceptive Pathways & Primary Sites of Action of Analgesics**

- **Trigeminal**
- NMDA-Channel Blockers
- Ketamine
- Methadone

**Integrative (non-pharmacological) therapies**

**Stimulation of inhibiting GABA system**

**Injury**

**NSAIDs**

**Inhibitors of excitatory glutamate systems:**

- Gabapentin
- Pregabalin
- Carbamazepine
- Valproate

**TCA SSRI Methadone Tramadol**

**Inhibition of glutamatergic neurotransmission**

**GABA-Antagonists**

**Benzodiazepines**

**Sodium-channel blockade**

**carbonic anhydrase inhibitors**

**Sodium-channel blockers**

**Bisphosphonates**

**Baclofen**

**Methadone**

**Tramadol**

**Ketamine**

**NSAIDs**

**Acetaminophen (Paracetamol)**

**Carbamazepine**

**Valproate**

**TCA**

**SSRI**

**Methadone**

**Tramadol**

**Ketamine**

**Methadone**

**Tramadol**

**Ketamine**

**Methadone**

**Tramadol**

**Ketamine**

**Methadone**

**Tramadol**

**Ketamine**

**Methadone**

**Tramadol**
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 (1) 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

Transition from acute to chronic pain

- Chronic post surgical pain (CPSP) after Surgery: last at least 2 months, other causes were excluded

- 1 year after surgery, 22% of children developed moderate to severe CPSP with minimal functional disability.

- 18% of children developed CPSP; associated with parental...
Communication with Patient / Family

- Pain is real!
- First “function” gets better, then “pain” (not other way around)
- Positive Expectation = Self-fulfilling prophecy

Communication with Patient / Family

What is the Hard Work...and non-negotiable...?

- **Physical Therapy**
  - Daily home exercise
- **Integrative Medicine**
  - Self-Hypnosis
  - Biofeedback
  - Progressive Muscle relaxation
  - Daily home exercise
  - Passive: Massage, Acupuncture
- **Psychology** (...if missing school)
- **Normalize Life**
  - Sports/exercise
  - Sleep-hygiene
  - Social: Having daily fun
  - School: Attending full-time (or school-re-entry plan)
- **Family Coaching**
- **Medications...???

Medications ???
Opioids & Chronic Pain

- **Lack of evidence**
  - Supporting long-term effectiveness
- Escalating **misuse** of prescription opioids including abuse and diversion
- Uncertainty about incidence of **adverse drug events**


- **endocrine dysfunction** (androgen deficiency)
- Immunosuppression & infectious disease
- Opioid-induced hyperalgesia
- Xerostomia
- Overdose
- Falls & fractures
- Psychosocial complications

Opioids & Chronic Pain

- Updated Cochrane Review: Effectiveness/safety of long-term opioid therapy for lower back pain remains unproven
  

- Even after adjusting for substantial number of potential confounders, opioids were associated with worse functioning in back pain patients at 6-month follow-up
  

- Chronic lower back pain: Increase in opioid use associated with increase in depression, and increase in depression associated with increase in opioid dose
  

- 109 patients with chronic pain over 7 years: NO relation between opioid dose change and clinical pain score
  

Opioids in the absence of tissue injury or inflammation not indicated!
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


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%

Picker Systemwide: Pain controlled all the time

![Bar Chart]

Locations surveyed: Surgery, NICU, SCN, ICC, ED & Med/Surg, Critical Care

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

- The New York Times (Dec 16, 2015) essay by Dr. Stefan Friedrichsdorf “When a Baby Dies” [link]
- Video: Kiran Stordalen and Horst Rechelbacher Pediatric Pain, Palliative and Integrative Medicine Clinic Tour [link]
- “Children’s Comfort Promise: Doing everything possible to treat and prevent pain!” Eliminating Needle Pain in children (Feb 2015) Staff video [link]
- Short Movie Meet the Interdisciplinary Chronic Pain Clinic Team at Children’s Minnesota: LittleStars TV [link]
- 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 [link]
- 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) [link]
Further Training

10th Annual Pediatric Pain Master Class
- Minneapolis, Minnesota, USA | June 17-23, 2017

Education in Palliative & End-of-life Care (EPEC): Become an EPEC-Pediatrics Trainer
- Montréal, Québec, Canada | April 29-30, 2017 (Professional Development Workshop 04/28/17)

Contact CIPPC@ChildrensMN.org

Thank You