

When Acetaminophen is Not Enough: Opioid Management for the Hospitalized Child



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Disclosures



We have no relevant financial relationships to disclose

Objectives

Part 1

- Breakout session
- Review literature on acute pain management in the hospitalized child
- Review WHO Pediatric Guidelines
- Define types of pain

Parts 2 and 3

- Review opioids and associated pharmacokinetics
- Provide guidelines for titrating, converting and weaning opioids
- Review common pearls and pitfalls
- Provide resources

Audience Response Instructions

- Search for the session title in the mobile app using the search bar or in the agenda layout
- Select the session to open the session page and select “Live Polls”
- Answer the question under “Live Polls” by selecting your desired answer(s)
- Select “Finish” to submit your answer

BREAKOUT SESSION

Case:

Sally is a 14 year old female with no significant past medical history admitted for complicated bacterial PNA with pleural effusions who is suffering from pleuritic pain



Background

RESEARCH ARTICLE

Pain Prevalence and Treatment Patterns in a US Children's Hospital

Kyrie Shomaker, MD,¹ Shiril Dutton, PNP,² Melissa Mark, MD³

ABSTRACT

OBJECTIVE: Hospitalized children experience significant pain despite improvement efforts. This study was undertaken to better understand the epidemiology of acute pain in hospitalized children and the extent to which existing measures reveal targets for improving pain management.

METHODS: A cross-sectional survey was used to audit pain assessment, intensity, prevalence, source, and treatment hospital-wide on a single day in 2011. Chart audits were performed on patients aged 0 to 21 years. All patients had the option to participate in a structured interview about their pain experience.

RESULTS: The audit included 112 children, 47 of whom were interviewed. Pain prevalence

Background

RESEARCH ARTICLE

Pain Outcomes in a US Children's Hospital: A Prospective Cross-Sectional Survey

abstract

BACKGROUND AND OBJECTIVES: Pain in hospitalized children may be underrecognized and undertreated. The objective of this survey was to benchmark pain prevalence, intensity, assessment, and pharmacologic as well as integrative treatment of pain in inpatients in a US children's hospital.

METHODS: This was a single-day, cross-sectional survey and electronic medical record review of inpatients who received medical care at a pediatric hospital. Inpatients and emergency department patients were asked to report their experience with pain and its management during the previous 24 hours.

RESULTS: Of 279 inpatients listed on the morning census, 178 children and parents were located and completed the survey. Seventy-six percent had experienced pain during the previous 24 hours, usually acute or procedural pain, 12% of whom possibly suffered from chronic pain. Twenty percent of all children surveyed experienced moderate and 30% severe pain in that time period. The most pain reported by patients was caused by procedures (20%).

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KEY WORDS

pediatric, pain, audit, Lean, quality improvement, children's hospital

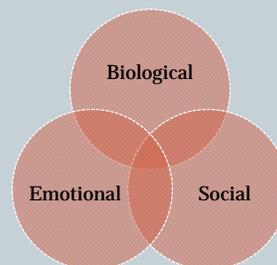
ABBREVIATIONS

CHC: Children's Hospitals and Clinics of Minnesota
NSAIDs: nonsteroidal anti-inflammatory drugs
DOI: 10.1097/01234567890

Definitions

- Pain

An unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage.



Classification of Chronic Pain, Second Edition, IASP Task Force on Taxonomy, edited by H. Merskey and N. Bogduk, IASP Press, Seattle, ©1994.

Types of Pain

- **Nociceptive**

- Tissue injury activates receptors (nociceptors) on skin or enclosed organs
- Receptors respond to heat, cold, vibration, stretch and chemical stimuli
- Somatic or visceral

- **Neuropathic**

- Nerve and structural damage in peripheral or central nervous system



WBC Pediatric Pain Guidelines 2016

Pain

- **Acute Pain**

- Sudden onset, felt immediately following injury.
- Severe in intensity but usually short lasting
- Secondary to injury that stimulate nociceptors and **generally goes away when injury heals**

- **Chronic Pain**

- Continuous or recurrent pain that is **lasting more than 12 weeks**
- Pain that persists beyond the normal expected time for tissue healing
- Secondary to disease, post injury or idiopathic causes

WHO Pediatric Pain Guidelines

- Published in 2012
- 172 page document regarding approach to pain in a child
- **Highlights:**
 - Pain often not recognized or ignored
 - Systemic Approach: By the child, By the clock, By the appropriate route, By the individual
 - Two step analgesic ladder
 - Codeine and tramadol no longer recommended

By the Clock

- When pain is constantly present, analgesics should be administered at regular intervals, monitoring for side effects
- Scheduled around the clock or basal infusion
- Scheduled reduces peaks and trough that occurs with PRN only and ensures steady blood level
- Encourage around the clock scheduling PLUS prn for breakthrough



By the Child

- Titrate opioids on individual basis
- With analgesic dosing, no sedation expected
- Effective dose is the dose that relieves pain
- Different children may respond differently to the same dose
- Dose of strong opioids: limited by side effects/toxicities; need monitoring and treatment side effects
- Asses pain frequently



By the Appropriate Route

- Difference between onset of action and peak vs. effective analgesia
- Choose least invasive route
- Switch from IV to PO medications as soon as possible



Routes

Oral	Intranasal
Intravenous	Buccal
Subcutaneous	Nebulized
Sublingual	Transdermal
Rectal	



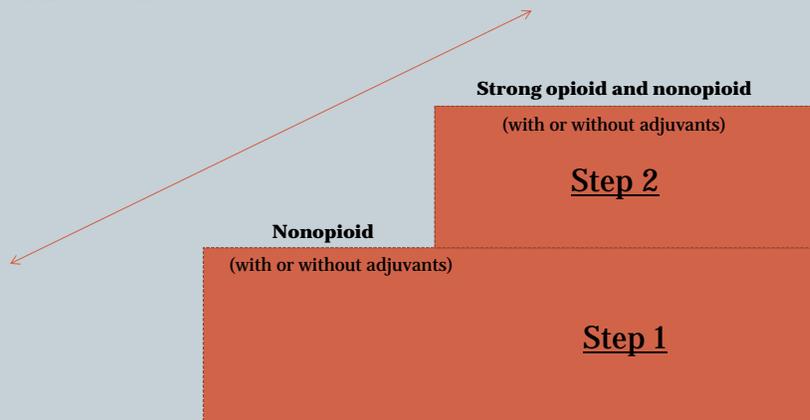
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Two Step Approach

- Choose analgesia according to level of severity
- Mild pain (pain score 1-3)- acetaminophen, ibuprofen, naproxen (and IV equivalents)
- Moderate (score 4-7) to severe pain (score 8-10)-opioid
- Bidirectional

Bidirectional Two Step Ladder

Adapted from WHO Guidelines



Why We Shouldn't Use Codeine and Tramadol

- Codeine is a prodrug that is then converted into the active metabolite morphine
- Variability of the enzyme CYP2D6 in individuals makes differences in its conversion unpredictable
- Percentage of poor metabolizers can vary by ethnic groups anywhere from 1% to 30%, resulting in ineffective treatment of pain for some
- On the other hand, ultra metabolizers are at higher risk for severe opioid toxicity
- Tramadol has a similar risk to codeine in terms of ultra rapid metabolizers

WHO Pediatric Pain Guidelines 2012

Parts 2: Opioid Management



Sally



- Sally is a 14-year-old female with no significant past medical history admitted for complicated bacterial pneumonia with pleural effusions s/p chest tube placement. She is receiving IV antibiotics and is stable on vapotherm, but continues to suffer from pleuritic pain.

Sally



- Because Sally is eating without difficulty, you decide to schedule ibuprofen with enteral morphine sulfate prn. She is opioid naïve. What would be your starting dose of morphine sulfate?
- Weight= 45 kgs

Audience Response Question: Sally's Pain

- What would be your starting dose of enteral morphine sulfate?

1) Morphine sulfate 1mg PO Q4h prn

2) Morphine sulfate 2mg PO Q4h prn

3) Morphine sulfate 5mg PO Q4h prn

4) Morphine sulfate 7.5mg PO Q4h prn

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Reasonable Options

- Morphine sulfate 5mg PO Q4h prn
- Could also consider:
 - Morphine sulfate basal infusion plus demand dose (PCA)
 - Morphine sulfate basal infusion plus oral prn dose
- Other suggestions?

Narcotic

- **Narcotic**
 - From the Greek, *narco*, to deaden
 - **a** : a drug (such as opium or morphine) that in moderate doses dulls the senses, relieves pain, and induces profound sleep, but in excessive doses causes stupor, coma, or convulsions
 - **b** : a drug (such as marijuana or LSD) subject to restriction similar to that of addictive narcotics whether physiologically (see physiological) addictive and narcotic or not

<https://www.merriam-webster.com/dictionary/narcotic>

Opioid

- **Opioid**

- **a** : any of a group of endogenous neural polypeptides (such as an endorphin or enkephalin) that bind especially to opiate receptors and mimic some of the pharmacological properties of opiates —called also *opioid peptide*
- **b** : a synthetic drug possessing narcotic properties similar to opiates, but not derived from opium; *broadly*

<https://www.merriam-webster.com/dictionary/opioid>

Opioid Analgesics

- **Act on opioid receptors**

- Mu
- Kappa
- Delta

- **Opioid receptors are responsible for different responses to opioids**

- Analgesia
- Euphoria
- Sedation
- Respiratory depression

Definitions

- **Tolerance**

- The need for increasing medication doses to obtain the same physiologic effect

- **Physical Dependence**

- The need to continue taking a medication to prevent withdrawal symptoms

- ✦ Both are physiologic adaptations to chronic opioid exposure

Definitions

- **Opioid Misuse**

- Opioid use in a manner other than directed or prescribed regardless of the presence or absence of harm or adverse effects

- **Addiction**

- Pattern of continued use with experience of, or demonstrated potential for harm



Vowles KE et al. Pain. 2015; 156(4):569-576

Opioids for Acute Pain

- Opioids do NOT have a maximum pharmacologic dose
- Appropriate dose is the dose needed to control pain with the fewest side effects
- Opioids for acute pain
 - Morphine
 - Oxycodone
 - Hydromorphone

Combination Medications

- Advantage
 - Less medication burden for children
- Disadvantage
 - Acetaminophen DOES have a ceiling – 15mg/kg/dose
- Combination medications
 - Acetaminophen/Hydrocodone
 - Acetaminophen/Oxycodone

Opioid Pharmacokinetics

Medication	Onset	Peak
Morphine IV	Rapid	5-20 minutes
Morphine PO/IR	15-60 minutes	30-60 minutes
Morphine PO/SR	60-90 minutes	3-4 hours
Oxycodone PO/IR	10-15 minutes	30-60 minutes
Oxycodone PO/SR	60 minutes	1-4 hours
Hydromorphone IV	Rapid	10-20 minutes
Hydromorphone PO	15-30 minutes	30-90 minutes
Fentanyl Patch	6 hours	24 hours

Audience Response Question: Back to Sally...

- Sally develops some mild pruritis after starting morphine. What would you do first?
 - 1) Rotate opioids
 - 2) Add diphenhydramine IV Q6h prn
 - 3) Add nalbuphine IV Q6h prn
 - 4) Start topical steroids

Opioid Induced Side Effects



Managing Adverse Effects of Opioids

Adverse Effect	Management
Nausea/Vomiting	Anti-emetics
Constipation	Laxatives Bowel stimulants Peripheral-acting opioid antagonists
Pruritus	Switch opioids Opioid antagonists or mixed agonist/antagonist Antihistamines
Urinary retention	Switch opioids Opioid antagonists or mixed agonist/antagonist

Managing Adverse Effects of Opioids

Adverse Effect	Management
Sedation	Decrease dose
Myoclonic Jerking	Decrease dose Switch opioids
Delirium/Confusion	Decrease dose Switch opioids Anti-psychotic therapy
Respiratory Depression	Hold opioid Supportive measures Consider naloxone

A Word about Rotating Opioids

- **Reasons to rotate**
 - Adverse effects are intolerable or irreversible
 - Need to change administration routes and current opioid is unavailable
 - Over sedation with poor analgesia
- **Must consider dose reduction for incomplete cross tolerance**



Part 3: Parenteral Opioids



Back to Sally...Hospital Day 1

- Receiving scheduled ibuprofen plus morphine PO Q4h prn
- Pain overall improved
 - Baseline somewhat improved (9-> 7)
 - Significant relief x 2 hrs after morphine (x 6 in 24 hours)
- Stooling regularly, no oversedation



Are you concerned about drug seeking?



Audience Response Question: What Would You Do Next?

- 1) Increase the enteral morphine *dose* but leave the same frequency
- 2) Increase the enteral morphine *frequency* but keep the same dose
- 3) Convert to morphine sulfate IV intermittent scheduled dosing
- 4) Convert to morphine sulfate PCA
- 5) Rotate to a different enteral opioid (ie dilaudid)

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Clinical Pearls

- End-of-Dose Failure-> Increase the frequency
- Pseudoaddiction vs drug seeking behavior
- Breakthrough dosing when receiving intermittent ATC opioids
 - 10% of total 24 hour dose given every 1-2 hours prn

Example:

- Morphine sulfate 5mg Q4h (30mg/day)
- Breakthrough dosing:
 - Morphine sulfate **3mg PO Q1-2h prn**

My Preference.....

- Start a morphine sulfate PCA



Why Parenteral Opioid Administration?

- **Standard of care for managing moderate to severe pain when:**
 - Oral/rectal route is unavailable and/or
 - Frequent dose adjustments are needed

Parenteral options:

- Morphine
- Hydromorphone
- Fentanyl
- Methadone

Patient Controlled Analgesia

- **Need to be alert, oriented and able to use the pump appropriately**
- **Nursing controlled analgesia (NCA)**
- **Family controlled analgesia (FCA)**

Continuous Infusions and Reaching Steady State

- It takes approximately **four half-lives** for opioids to reach steady state plasma concentration if given as an infusion

Drug	Time to reach steady state
Morphine	8 hours
Hydromorphone (dilaudid)	8 hours
Fentanyl	1.5 hours

PCA – Reassessment is Key

- **Reassess continuous infusion rate every 6-8 hours**
 - Check frequency of demand doses for guidance
 - Titrate the demand dose, the basal or both?
- **Adjustments should be individualized**

Pearls & Pitfalls of PCA Conversion

- Consider your starting point
- Adjustments in hourly rate based on:
 - Starting point OR
 - Opioid rotation
- If continuous infusion represents dosage increase:
 - Provide a **loading dose**

Audience Response Question: Back to Sally

- What would be your PCA starting basal infusion?
 - 1) Morphine sulfate IV 5mg/hr
 - 2) Morphine sulfate IV 3mg/hr
 - 3) Morphine sulfate IV 0.5mg/hr
 - 4) Morphine sulfate IV 2mg/hr

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Using the Conversion Table

Equianalgesic Doses

		New Agent (mg*)					
		Morphine IV	Morphine PO	Hydromorphone IV	Hydromorphone PO	Oxycodone PO	Fentanyl IV (mcg)
Current Agent (mg*)	Morphine IV		3	0.2	0.6	2	20
	Morphine PO	0.33		0.05	0.2	0.67	10
	Hydromorphone IV	5	15		3.5	10	100
	Hydromorphone PO	1	4	0.2		2.6	33
	Oxycodone PO	0.3	1	0.05	0.2		10
	Fentanyl IV (mcg)	0.05	0.1	0.01	0.03	0.1	

Multiply dose of current agent (left) by conversion factor for new agent (top).

When converting opioids, be sure to reduce dose by 25-50 percent to account for incomplete cross-tolerance.

* = dose increment in milligrams except where noted.

For example:

- **Step 1:** What's your starting dose
 - Morphine 5mg PO Q4h
- **Step 2:** Calculate total 24 hr dose
 - 5 mg x 6 = 30 mg (PO)
- **Step 3:** Convert to IV
 - 30mg PO x 0.33 = 10 mg IV
- **Step 4:** Calculate hourly dosing
 - 10mg/24 = 0.4mg/hr

Sally's Order

- Medication: Morphine Sulfate 1mg/1ml
- Basal infusion: 0.5 mg/hr
- PCA bolus: 0.5 mg
- Lockout interval: Every 15 minutes, max 4 boluses/hr

Back to Sally...Hospital Day 3

- She ultimately needed a VATs procedure
- Pain has increased following procedure
- Currently on:
 - Morphine sulfate PCA 0.5mg/hr plus 0.5mg demand dose every 15 minutes prn
- Pushing button frequently (2-3 x per hour for the last 6 hours)
- What do you want to do next?

Typical Titration Recommendations

- **Titration:**
 - If receiving more than 2 PCA boluses per hour for more than 4 consecutive hours **AND:**
 - ✦ If unrelieved pain **AND**
 - ✦ If no oversedation or dose-limiting side effects-> **increase PCA by 50-100%**
 - Currently at 0.5mg/hr plus 0.5mg demand dose

Step 1: Increase to 1mg/hr and PCA bolus to 1mg
Step 2: Increase to 1.5mg/hr and bolus to 1.5mg

Troubleshooting

- Resident is called after nurse is concerned that patient is **oversedated**
- **On exam:**
 - Sleeping comfortably, 100% on RA
 - Arousable but with slurred speech and drifting off to sleep mid-sentence
 - Regular respirations

Audience Response Question: Troubleshooting



- What would you advise the resident to do next?
 - 1) Rotate to hydromorphone (dilaudid)
 - 2) Discontinue morphine infusion
 - 3) Hold infusion until she wakes up and decrease the dose by 50%
 - 4) Give a dose of naloxone (narcan)

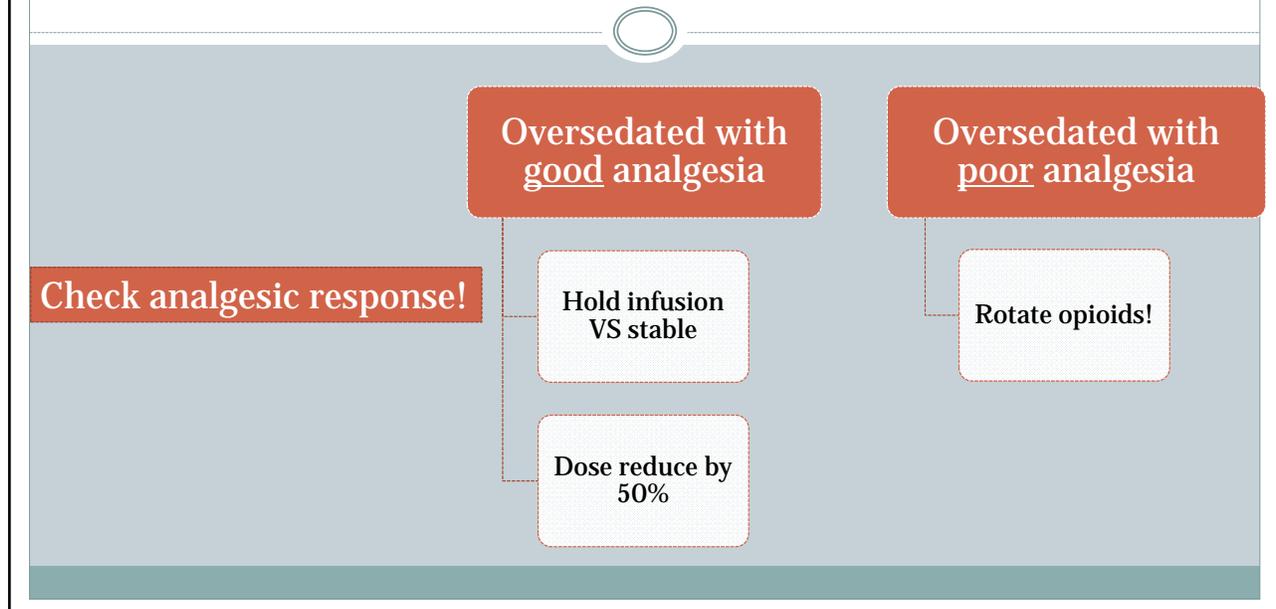
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Opioids and Oversedation



Assessing Sedation From Opioids

PASERO OPIOID-INDUCED SEDATION SCALE (POSS) WITH INTERVENTIONS

- S = Sleep easy to arouse Acceptable;
- 1 = Awake and alert Acceptable;
- 2 = Slightly drowsy, easily aroused Acceptable;
- 3 = Frequently drowsy, arousable, drifts off to sleep during conversation Unacceptable;
- 4 = Somnolent, minimal or no response to verbal and physical stimulation Unacceptable.

• Copyright 1994, Chris Pasero.

More Troubleshooting with a PCA...

- Patient has poor pain control and no adverse effects?
- Patient having adverse effects (constipation, urinary retention, pruritis)?
- Oversedation with good analgesia?
- Oversedation with poor analgesia?
- Pain relief except during periods of activity?

Weaning...

- If on scheduled opioids for **>5 days**, recommend weaning by 10-20% of the total maximum 24 hour dose
 - Could be as frequent as daily

Sally's wean...

- Morphine sulfate PCA 2mg/hr
 - Wean infusion by 0.2 – 0.4 mg/hr per day
 - ✦ Day 1: 1.8 mg/hr
 - ✦ Day 3: 1.6mg/hr
- What do you do with the demand dose?
 - 2mg IV Q15 min prn

Monitor WAT-1 scores!!

Withdrawal Assessment Tool- 1

WITHDRAWAL ASSESSMENT TOOL VERSION 1 (WAT-1)
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Patient Identifier		Date:							
		Time:							
Information from patient record, previous 12 hours									
Any loose/watery stools	No = 0 Yes = 1								
Any vomiting/wretching/gagging	No = 0 Yes = 1								
Temperature > 37.8°C	No = 0 Yes = 1								
2 minute pre-stimulus observation									
State	SBS ¹ ≤ 0 or asleep/awake/calm = 0 SBS ¹ > +1 or awake/distressed = 1								
Tremor	None/mild = 0 Moderate/severe = 1								
Any sweating	No = 0 Yes = 1								
Uncoordinated/repetitive movement	None/mild = 0 Moderate/severe = 1								
Yawning or sneezing	None or 1 = 0 ≥ 2 = 1								
1 minute stimulus observation									
Startle to touch	None/mild = 0 Moderate/severe = 1								
Muscle tone	Normal = 0 Increased = 1								
Post-stimulus recovery									
Time to gain calm state (SBS ¹ ≤ 0)	< 2min = 0 2 - 5min = 1 > 5 min = 2								
Total Score (0-12)									

Last Minute Reminders...

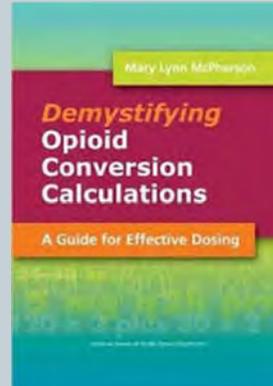
- No max dosing for opioids
- 2 main reasons to rotate opioids:
 - Intolerable adverse reaction
 - Oversedation with **poor** analgesia
- Dose reduce for incomplete cross-tolerance!
- Use conversion tables
 - Changing routes or drugs
- Start a bowel regimen
- Wait at least 12-24 hours before titrating your basal infusion

A Few More Reminders....

- Reserve parenteral opioids for patients who:
 - Unable to tolerate PO
 - Need immediate relief or a PCA
- Consider pain trajectory
- Manage oversedation appropriately
 - Consider analgesic response
- Use WAT-1 scores when weaning

Great Resources

- McPherson, ML. Demystifying Opioid Conversion Calculations: A Guide for Effective Dosing.
- www.globalrph.org



THANK YOU!

THE LOUIS CK PAIN CHART



NORMAL
DISCOMFORT



DISAPPOINTED



DISGUSTED
WITH SELF



DISGUSTED
WITH SELF AND WORLD



@#\$%*&!

CHOOSE THE FACE THAT BEST DESCRIBES YOUR PAIN

VULTURE