

ANALGESICS FOR PEDIATRIC PAIN TREATMENT

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- Definition
- Classification
- Assessment
- Pharmacology of different analgesics

Definition of Pain

- *International Association for the Study of Pain*
 - An unpleasant sensory and emotional experience arising from actual or potential tissue damage or described in terms of such damage

Barriers to Pediatric Pain Control

- Children, especially infants, do not feel pain the way adults do
- Lack of routine pain assessment
- Lack of knowledge in pain treatment
- Fear of adverse effects of analgesics, especially respiratory depression and addiction
- Preventing pain in children takes too much time and effort

Classification of Pain

Nociceptive

- Somatic
 - Bone, joint, muscle, skin, or connective tissue
 - Well localized
 - Aching & throbbing
- Visceral
 - Visceral organs such as GI tract
 - Poorly localized
 - Cramping

Neuropathic

- Central
 - Injury to peripheral or central nervous system causing phantom pain
 - Dysregulation of the autonomic nervous system
- Peripheral
 - Peripheral neuropathy due to nerve injury
 - Pain along nerve fibers

Pain Assessment

- Obtain a detailed assessment of pain
 - Quality, location, duration, intensity, radiation, relieving & exacerbating factors, & associated symptoms
 - Many scales available
 - NIPS (Neonatal Infant Pain Scale)
 - FLACC scale (Face, Legs, Activity, Cry Consolability)
- Directly ask child when possible
- Pain can be multi-dimensional and therefore, tools can be limited

Assessment in Neonates & Infants

- Challenging
- Combines physiologic and behavioral parameters
- Many scales available
 - NIPS (Neonatal Infant Pain Scale)
 - FLACC scale (Face, Legs, Activity, Cry Consolability)

Neonatal Infant Pain Scale (NIPS)

Table II – Neonatal Infant Pain Scale

NIPS	0 point	1 point	2 points
Facial expression	Relaxed	Contracted	–
Cry	Absent	Mumbling	Vigorous
Breathing	Relaxed	Different than basal	–
Arms	Relaxed	Flexed/stretched	–
Legs	Relaxed	Flexed/stretched	–
Alertness	Sleeping/calm	Uncomfortable	–

Maximal score of seven points, considering pain ≥ 4 .

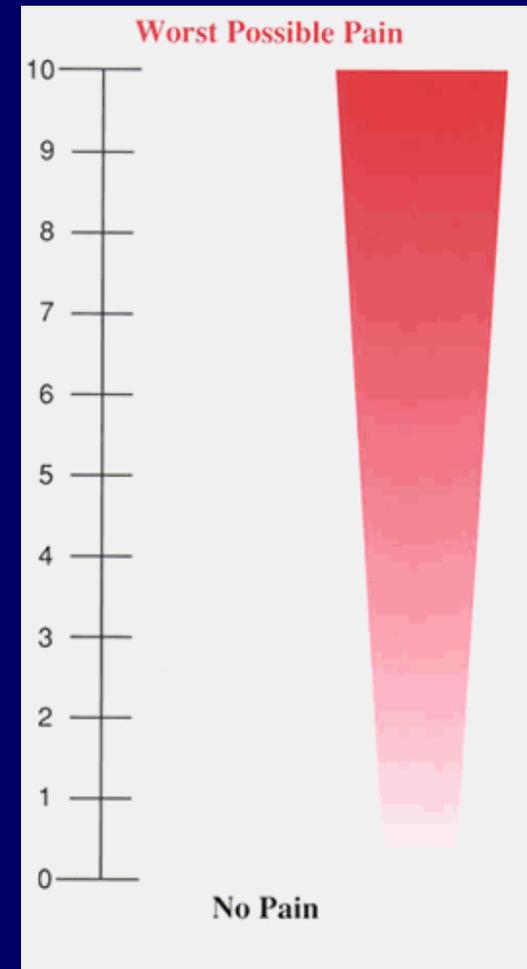
FLACC scale

Behavioral Observation Pain Rating Scale

Categories	Scoring		
	0	1	2
Face	No particular expression or smile; disinterested	Occasional grimace or frown, withdrawn	Frequent to constant frown, clenched jaw, quivering chin
Legs	No position or relaxed	Uneasy, restless, tense	Kicking, or legs drawn up
Activity	Lying quietly, normal position, moves easily	Squirming, shifting back and forth, tense	Arched, rigid, or jerking
Cry	No crying (awake or asleep)	Moans or whimpers, occasional complaint	Crying steadily, screams or sobs, frequent complaints
Consolability	Content, relaxed	Reassured by occasional touching, hugging, or talking to. Distractable	Difficult to console or comfort
<p>Each of the five categories (F) Face; (L) Legs; (A) Activity; (C) Cry; (C) Consolability is scored from 0-2, which results in a total score between 0 and 10.</p>			

Children between 3-8 years

- Usually have a word for pain
- Can articulate more detail about the presence and location of pain; less able to comment on quality or intensity
- Examples:
 - Color scales
 - Faces scales



Children with Cognitive Impairment

- Often unable to describe pain
- Altered nervous system and experience pain differently
- Use behavioral observation scales
 - e.g. FLACC
- Can apply to intubated patients

Analgesics



Principles of Pharmacology

- Consider patient's age, associated medical problems, type of pain, & previous experience with pain
- Choose type of analgesia
- Choose route to control pain as rapidly and effectively as possible
- Titrate further doses based on initial response
- Anticipate side effects
- Recognize synergistic effects

Routes of Analgesics

- Administer analgesia through most painless route
 - Avoid IM injections
 - Oral and Intravenous routes are preferred
 - **Oral route** for mild to moderate pain
 - **Intravenous route** for immediate pain relief and severe pain

TABLE 1. AGE-RELATED PHYSIOLOGICAL TRENDS RELEVANT TO ANALGESIC-DRUG ACTION.*

PHYSIOLOGICAL SYSTEM	AGE-RELATED TREND	CLINICAL IMPLICATIONS
Body compartments	Neonates: decreased fat, decreased muscle, increased water; increased volume of distribution for water-soluble drugs	Increased duration of action for some water-soluble drugs; increased dosing interval
Plasma protein binding	Neonates: decreased concentrations of albumin and α_1 -acid glycoprotein	Increased unbound concentrations for highly protein-bound drugs; increased potential for overdose or toxicity
Hepatic-enzyme systems for drug metabolism	Neonates and infants: immature hepatic cytochrome P-450 subtypes and glucuronyl transferases Children 2–6 yr: increased hepatic mass	Neonates and infants: decreased metabolic clearances; decreased infusion rates or increased dosing intervals Children 2–6 yr: increased metabolic clearance; increased infusion rates or decreased dosing intervals
Renal filtration and excretion of drugs and their metabolites	Neonates and infants: decreased glomerular filtration rates	Neonates and infants: accumulation of renally excreted drugs or active metabolites; decreased infusion rates or increased dosing intervals
Metabolic rate, oxygen consumption, and respiratory function	Neonates and infants: increased oxygen consumption; increased ratio of oxygen consumption to functional residual capacity; decreased fatigue-resistant (type 2) diaphragm fibers; decreased airway caliber; increased resistive work of breathing; decreased pharyngeal and lingual muscle control; decreased rigidity of larynx and subglottic trachea; decreased ventilatory responses to oxygen and carbon dioxide; functional residual capacity near alveolar closing volume	Neonates and infants: respiratory pauses or apnea lead more rapidly to hypoxemia; increased rate of onset and offset of inhalational anesthetics; increased risk of atelectasis or respiratory failure if illness or surgery imposes additional work of breathing; increased risk of hypoventilation due to the combined effects of decreased ventilatory reflexes and responses to opioids or sedatives

*Differences in physiological variables are expressed as increased or decreased relative to the comparable weight-scaled variables in adults. Differences in doses (normalized per kilogram of body mass) or in infusion rate (normalized in milligrams per kilogram per hour) are expressed as increased or decreased relative to comparable variables in adults.

- Step 1 (1-3): acetaminophen, NSAIDs
- Step 2 (4-6): codeine, tramadol, hydrocodone, oxycodone
- Step 3 (7-10): morphine, oxycodone, fentanyl, methadone

Non-opioid Analgesics

- Mild to moderate pain
- No side effects of respiratory depression
- Highly effective when combined with opioids

- Acetaminophen
- NSAIDs
- COX-2 inhibitors
- Aspirin
 - No longer used in pediatrics

Acetaminophen

- Antipyretic
- Mild analgesic
- Administer PO or PR
- Pediatric Oral dose 10-15 mg/kg/dose every 4 hr
 - Infant dose is 10-15 mg/kg/dose every 6-8 hr
 - Adult dose 650 mg-1000 mg/dose
- Onset 30 minutes

Acetaminophen

- Per rectum dose 40 mg/kg once followed by 20 mg/kg/dose every 6 hours
 - Uptake is delayed and variable
 - Peak absorption is 60-120 minutes
- Maximum daily dosing
 - Infants: 60-75 mg/kg/day
 - <60 kg: 100 mg/kg/day
 - >60 kg: 4 grams/day

Side Effects of Acetaminophen

- Generally a good safety profile
 - Do not use in hepatic failure
- Causes hepatic failure in overdose
 - Combination medicines
 - Infant's Acetaminophen drops 80 mg/0.8 mL;
120mg/ml
 - Children's Acetaminophen suspension 160 mg/5 mL

NSAIDs

- Antipyretic
- Analgesic for mild to moderate pain
- Anti-inflammatory
 - COX inhibitor → Prostaglandin inhibitor
- Platelet aggregation inhibitor

NSAIDs: Ibuprofen

- Dose 10 mg/kg/dose every 6 hours
 - Adult dose 400-600 mg/dose every 6 hours
- Onset 30-45 minutes
- Maximum daily dosing
 - <60 kg: 40 mg/kg
 - >60 kg: 2400 mg
 - May use higher doses in rheumatologic disease

NSAIDs: Ketorolac

- Intravenous NSAID (also available P.O.)
- Dose 0.5 mg/kg/dose every 6 hours
- Onset 10 minutes
- Maximum I.V. dose 30 mg every 6 hours

- Monitor renal function
- Do not use more than 5 days
 - Significant increase in side effects after 5 days

Side Effects of NSAIDs

- Gastritis
 - Prolonged use increases risk of GI bleed
 - Still rare in pediatric patients compared to adults
 - NSAID use contraindicated in ulcer disease
- Nephropathy
- Bleeding from platelet anti-aggregation
 - Increased risk versus benefit post-tonsillectomy
 - NSAID use contraindicated in active bleeding

COX-2 inhibitors

- Selectively inhibits Cyclooxygenase-2 which reduces risk of gastric irritation and bleeding
- Same risk for nephropathy as non-selective COX inhibitors
- Shown to have increased cardiovascular events in adults
- More studies needed in pediatric patients
 - COX-2 inhibitors used in rheumatologic diseases

Opioids Analgesics

- Moderate to severe pain
- Various routes of administration
- Different pharmacokinetics for different age groups
 - Infants younger than 3 months have increased risk of hypoventilation and respiratory depression
- Low risk of addiction among children

Principles of Opioid Use

- Work at opioid (μ) receptors in the CNS and peripheral nervous system
- Each opioid has different affinities for different receptors, so there is variability in response among patients

Side Effects of Opioids

- All opioids have side effects that should be anticipated & managed
 - Respiratory depression
 - Nausea, vomiting
 - Constipation
 - Pruritis
 - Urinary retention

Opioids

- Codeine
- Oxycodone
- Morphine
- Fentanyl
- Hydromorphone
- Methadone

Codeine

- Oral analgesic (also anti-tussive)
- Weak opioid
 - Used often in conjunction with acetaminophen to increase analgesic effect
- Metabolized in the liver and demethylated to morphine
 - Some patients ineffectively convert codeine to morphine so no analgesia is achieved
- Dose 0.5-1 mg/kg every 4-6 hours

Oxycodone

- Oral analgesic
- Mild to moderate pain
- Hepatic metabolism to noroxycodone and oxymorphone
- Can be given alone or in combination with acetaminophen
- Dose 0.05-0.15 mg/kg every 4-6 hours
- Maximum 5-10 mg every 4-6 hours

Morphine

- Available orally, sublingually, subcutaneously, intravenous, rectally, intrathecally
- Moderate to severe pain
- Hepatic conversion with renally excreted metabolites
 - Use in caution with renal failure
- Duration of I.V. analgesia 2-4 hours
 - Oral form comes in an immediate and sustained release
- Dose dependent on formulation
- I.V. Dose 0.05-0.2 mg/kg/dose every 2-4 hours
- Onset 5-10 minutes
- Side effect of significant histamine release

Fentanyl

- Available intravenous, buccal tab, lozenge and transdermal patch
- Severe pain
- Rapid onset, brief duration of action
 - With continuous infusion, longer duration of action
- I.V. Dose 1 mcg/kg/dose every 30-60 minutes
- Side effect of rapid administration may produce glottic and chest wall rigidity

Other Opioids

- Hydromorphone
 - 5 x more potent than Morphine (IV)
 - Available P.O. or I.V.
 - Used in patients with renal insufficiency
- Methadone
 - Very long half-life with slow peak
 - Good for steady level of analgesia
 - Accumulates slowly and takes days to reach steady state

Naloxone

- Opioid antagonist
- 1 ampule = 0.4 mg/mL
- Use when unresponsive to physical stimulation, shallow respirations (<8 breaths/min), pinpoint pupils
- Stop Opioid
- Mix Naloxone 1 ampule with NS 9 mL = 40 mcg/mL
 - For <40 kgs: Naloxone ¼ ampule with NS 9 mL = 10 mcg/mL
- Administer slowly and observe response
 - 1-2 mcg/kg/min
- Discontinue naloxone as soon as patient responds
- Duration 30-45 minutes
 - Monitor the patient; repeat doses may be needed

Monitor Patients receiving Opioids

- Close observation of all patients receiving opioids
 - Routine vital signs
 - Sedation scales when indicated
- Particular close attention to patients:
 - History of OSA
 - Craniofacial anomalies
 - Infants who are younger than 6 months or older infants with history of apnea or prematurity
 - Opioid-naïve patients with continuous infusions

Local Anesthetics

- For needle procedures, suturing, lumbar puncture, etc.
- Topical or infiltration
- Acts by blocking nerve conduction at Na-channels
- If administered in excessive doses, can cause systemic effects
 - CNS effects of perioral numbness, dizziness, muscular twitching, seizures & cardiac toxicity
 - Aspirate back before injecting to avoid direct injection into blood vessels
 - Calculate maximum mg/kg dose to avoid overdose
- Buffering lidocaine can help with pain of infiltration
 - 9 mL lidocaine mixed with 1 mL sodium bicarbonate

Anesthesia

- Regional
 - Blocks afferent pathways to CNS
 - Good for post-operative pain relief
 - Epidural and caudal anesthesia
 - Peripheral nerve blocks
- General

THANK YOU!



References

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