Management of Chronic Pain in Children

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“Cure sometimes, treat often, comfort always.”
—Hippocrates

Objectives:

1. Describe the pain pathway and pathophysiology of pain control
2. Recognize and categorize pain in children
3. Develop an individualized pain management plan for children with chronic pain

The number of children admitted with chronic pain has increased by 831% from 2004 to 2010.

Common Myths about Pain

- Children do not feel pain to the same degree as adults.
- It is not possible to adequately measure pain in cognitively impaired patients.
- Physical manifestations of pain are more important than self-report measurements.
- Pain does not exist in the absence of detectable tissue damage.
- Pain without an obvious source is usually psychogenic.

Common Myths about Pain

- The same stimulus produces the same degree of pain in all individuals.
- Analgesic therapy should not be started until the cause of pain is established.
- Use of opioids causes all patients to become addicted to them.
- Aggressive pain management is synonymous with prescribing opioids.
General Principles of Pain Management

- Assessment of pain in children must be tailored to the child’s developmental stage.
- The gold standard of pain measurement is patient self-report.
- Trust of health-care practitioners is critical to obtaining honest reports of pain from children.
- It is important to ask the child about pain regularly and document and reassess the child’s pain following an intervention.

Physiologic indicators, such as changes in pulse or blood pressure, may not be reliable indicators of pain in a chronically or critically ill child.

- Behavioral indicators, such as facial grimacing or crying, are unreliable and may be absent in the presence of chronic pain or critical illness.
- Children who have pain may use play or sleep as coping mechanisms; these behaviors do not mean the child is free of pain.

Pain Pathway

- Transduction
- Transmission
- Modulation
- Perception

Gate Control Theory

- Endogenous ability to reduce or increase the degree of perceived pain
- “Gate” located in the dorsal horn of the spinal cord.
- Acts on signals from the ascending and descending systems and weighs all of the inputs.
- Can be opened or closed by pharmacologic manipulation, transduction, transmission and modulation, and psychological intervention.
Pain Assessment

• Pain assessment is NOT a one-time phenomenon.

• Joint Commission standards:
  “pain is considered to be the fifth vital sign and should be assessed initially and reassessed on a scheduled and regular basis.”

Individualized Numeric Rating Scale
Neuropathic Pain

- Pain due to damaged or dysfunctional nerves.
- Both peripheral and central mechanisms:
  - Changes in the dorsal horn after nerve injury include reorganization.
  - Modulation in sensory input.
  - Enlargement of the second-order neuron’s receptive field.
  - Alteration in opioid receptivity.

Central Sensitization

- Excessive nociceptive nerve signals bombarding the central nervous system from the periphery.
- Long-term changes occur in the central nervous system.
- Persistent amplification of pain signals.

Dysfunctional Pain

- Pain and abnormal sensitivity not associated with noxious stimulus, tissue damage, inflammation, or identifiable lesion to the nervous system.
- Includes fibromyalgia, tension-type headaches, migraines, and irritable bowel syndrome.
- High prevalence of associated co-morbid conditions.

Dysfunctional Pain

- Need to help patient understand that persistent pain signals do not indicate ongoing tissue damage. This belief results in fear of movement, physical activity, and the future.
- It may be necessary to educate the patient that pain does not equal harm and that appropriate physical activity is important.
Patients often believe that medicine has a cure for their problems.
For many, accepting that chronic pain can be treated but not necessarily cured is a gradual process.
Encouragement to continue to be engaged in life as pain is being managed and not wait for a “cure” is often necessary.

Fibromyalgia
Patients typically present with the following complaints:
- Chronic widespread muscular pain
- Chronic fatigue
- Widespread tenderness (hyperalgesia)
Many people with fibromyalgia also experience additional symptoms, such as the following:
- Morning stiffness
- Headaches
- Irritable bowel syndrome
- Cognitive and memory problems (often called “fibro fog”)
- Irritable bladder

Treatment is with analgesics and usually includes an antidepressant.
Pregabalin has shown to be effective in treating some patients with fibromyalgia.
Exercise programs, analgesics, and behavioral therapy.
AVOID use of opioids.

Pain Team
- Anesthesiologists
- Clergy
- Complementary and Alternative Medicine Specialists
- Neurologists
- Nurses
- Physical Medicine and Rehabilitation Specialists
- Physical or Occupational Therapists
- Psychiatrists
- Psychologists
- Social Workers

Referral to a Mental Health Professional
- Suicidal ideation with or without intent or plan
- Anergia
- Persistent anhedonia
- Loss of appetite
- Sleep disturbance
- Anxiety or panic
- Prolonged difficulty accepting the condition
- Angry outbursts toward self or others
WHO Principles for Pharmacological Management

- Use a two-step strategy
- Dose at regular intervals “by the clock”
- Use the appropriate route of administration “by the mouth”
- Adapt treatment to the individual child “by the individual”

WHO two-step strategy

Moderate to Severe
Morphine is the medicine of choice, although other strong opioids should be considered and made available to ensure an alternative to morphine in case of intolerable side-effects.

No Pain

Mild

Acetaminophen and ibuprofen are the medicines of choice.

Acetaminophen

- Also known as paracetamol
- A nonsteroidal anti-inflammatory drug with potent antipyretic and analgesic actions but with very weak anti-inflammatory activity.
- Lacks the typical actions of NSAIDs, such as antiplatelet activity and gastrototoxicity
- Can be administered intravenously

NSAIDS

- NSAIDs are particularly good for bone pain and incident pain, or the type of pain that is provoked by activity (e.g., walking).
- All types of pain may respond to NSAIDs; however, visceral pain is probably less responsive than somatic pain, and neuropathic pain is often unresponsive.
- Ketorolac and ibuprofen can be given intravenously.

Opioids

- Opioid analgesics are considered to be a mainstay in the treatment of moderate to severe pain that does not respond to non-opioids alone, because they:
  - Are effective,
  - Are fairly easy to titrate,
  - Have a favorable risk-to-benefit ratio.

Opioids

- Opioids can exhibit their analgesic effects by acting on both peripheral and central mu, kappa, and delta opioid receptors.
- Inhibit the transmission of nociceptive input from the periphery to the spinal cord
- Activate the inhibitory pathways that modulate transmission
- Alters limbic system activity.
- May also work peripherally in areas of inflammation
The Language of Analgesia

- Opioid vs. Narcotic
- Medication vs. Drug

Addiction

- Addiction is a chronic neurobiologic disease with genetic, psychosocial, and environmental influences.
- It is characterized by
  - impaired control over drug use
  - compulsive use
  - continued use despite harm
  - need to use for effects other than pain relief
  - craving

Tolerance

- Process of decreasing effect of a drug over time, requiring increased dose to achieve same level of efficacy
  - Can be evident after a few days of treatment
  - First indication: decrease in duration of analgesia, then decrease in analgesic effect
- Not always the reason for need for dose escalation, should consider differential diagnosis

Tolerance

- Easily overcome by up titrating opioid
- Should not withhold opioid for fear of producing tolerance or reaching dose beyond which no further analgesia can be achieved
- Tolerance to non-analgesic side-effects does occur

Physical dependence

- Physical dependence is a physiologic adaptation that occurs in patients receiving opioid analgesics.
- Characterized by the development of withdrawal symptoms when a medication is stopped or decreased abruptly
- Expected in patients receiving opioid analgesics for more than a few days.
- Withdrawal can be avoided by tapering the dose when discontinuing treatment.
**Pseudoaddiction**

- A term used to describe behavior that appears to be addictive, “drug-seeking” behavior, but is actually an effort to obtain pain relief by a nonaddicted patient who is not receiving adequate analgesia.

**Opioid Side Effects**

- Constipation
- Pruritus
- Sedation
- Nausea and vomiting
- Urinary retention
- Mental clouding
- Addiction
- Myoclonus
- Respiratory depression.

**Opioid-induced Nausea**

- Dopamine-blocking agents
  - Prochlorperazine
  - Haloperidol
  - Metoclopramide
- 5-HT3 receptor antagonists
  - Ondansetron

**Myoclonus**

- Sudden unexpected repetitive, but nonrhythmic jerks of unrelated muscle groups.
- Treatment approach consists of:
  - opioid rotation if possible
  - suppressed with a number of agents (baclofen, valproic acid, clonazepam, gabapentin).

**Opioid-induced Hyperalgesia**

- Refers to a phenomenon whereby opioid administration results in a lowering of pain threshold, clinically manifested as apparent opioid tolerance, worsening pain despite accelerating opioid doses, and abnormal pain symptoms.
Respiratory Depression

- Opioids typically produce a concentration-dependent shift in the carbon dioxide response curve. When this shift becomes great enough, clinical expression of respiratory depression occurs, usually as a decrease in respiratory rate.
- Usually with clinically appropriate doses, compensation occurs, and respiratory rate does not decline.

Coding event

- In the event of a cardiorespiratory event, a patient’s response may be exaggerated due to the presence of opioid concentrations in the bloodstream.
- Even in the absence of clinical signs, there may still be residual effects on respiratory reserve after tolerance develops, and this must be kept in mind with patients on chronic opioids.

Naloxone

- Overly aggressive administration of naloxone in a patient on chronic opioid therapy can cause severe withdrawal syndrome.
- Children and patients who weigh less than 40 kg should have 0.1 mg of naloxone diluted in 10 mL of saline to make a 10 mcg/mL solution, given at 0.5 mcg/kg every 2 minutes.

Morphine

- Gold standard for moderate or severe pain
- Schedule 2 controlled substance

Codeine

- WHO does not recommend its use.
- US FDA Black Box warning for use after tonsillectomy
- Highly variable metabolism makes it unreliable
- Up to 30% children poor metabolizers. Some children are ultra-rapid metabolizers.
- Active metabolite is morphine.
**Hydrocodone**

- Only available in combination with acetaminophen or ibuprofen
- Schedule 3 controlled substance makes it easier to prescribe
- Preferred over codeine

**Fentanyl**

- Patch can be used in some cancer and chronic non-malignant pain
- Patches are not for opioid naïve children

**Sustained-release Opioids**

- Children often cannot swallow pills
- Even lowest dosages of sustained release products may be too high for children
- High rates of gastrostomy tubes in pediatric palliative care population necessitate liquid formulations

**Methadone**

- Used in chronic pain
- Long half-life therefore longer time to steady state
- Should not be used for breakthrough pain
- Has NMDA receptor activity
- Only liquid long-acting formulation

**Tramadol**

- Tramadol is unique in that it has a dual mechanism of action.
  - weak agonist at the mu opioid receptor
  - inhibits reuptake of norepinephrine and serotonin
- Tramadol is typically used for mild to moderate pain
- WHO does not recommend for children
Ajuvants

- Antidepressants - amitriptyline, nortriptyline
- Anticonvulsants - valproic acid, phenytoin
- Anxiolytics - benzodiazipines
- Corticosteroids – dexamethasone
- Anesthetics - lidocaine, ketamine
- Gabapentinoids – gabapentin, pregabalin
- Alpha-agonist – clonidine, guanfacine
- SNRI - duloxetine

Corticosteroids

- Often used in palliative care, where they have a number of beneficial effects, including
  - pain reduction,
  - improved appetite
  - weight gain
  - antiemetic action
  - mood elevation.
- Steroids are used in the treatment of neuropathic pain due to cord compression, brachial or lumbosacral plexus invasion, or peripheral nerve infiltration.

Anticonvulsants

- Used for some neuropathic pain conditions to relieve lancinating or stabbing pain.
- Suppress discharge in pathologically altered neurons, thus inhibiting neural hyperexcitability

Tricyclic Antidepressants

- Useful agents for neuropathic pain, cancer pain, and nonneuropathic pain with certain symptoms (e.g., insomnia, depression, or visceral spasm).
- Suppress pain-signaling through local anesthetic-like effects at sodium channels in neural membranes.
- Inhibit reuptake of norepinephrine, serotonin, and dopamine at synapses, which may increase their analgesic effects, as well as improve mood favorably.

Ketamine

- Acts at the NMDA receptor
  - excitatory glutamatergic receptor present spinal and supraspinal
  - In chronic pain states prolonged nociceptive stimulation causes activation and upregulation of the NMDAR at dorsal horn synapses resulting in enhanced and amplified trafficking of pain signals to the brain (central sensitization).
Useful Resources