Prescription Pain Management

University of Hawai‘i Hilo Pre-Nursing Program
NURS 203 – General Pharmacology
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Objectives

- Understand how to perform a pain assessment
- Know which medications fit into which pain management classes
- Know the general effects and adverse effects of the medications/classes of medications
Pain Assessment

PAIN ASSESSMENT TOOL

<table>
<thead>
<tr>
<th>Score</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>No Pain</td>
</tr>
<tr>
<td>1-3</td>
<td>Mild</td>
</tr>
<tr>
<td>4-6</td>
<td>Moderate</td>
</tr>
<tr>
<td>7-9</td>
<td>Severe</td>
</tr>
<tr>
<td>10</td>
<td>Very Severe</td>
</tr>
<tr>
<td></td>
<td>Worst Pain Possible</td>
</tr>
</tbody>
</table>

0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10
Pain Assessment

- Babies
  - Respond to changes
    - Crying
    - Temperature
    - Blood pressure
    - Heart rate
    - Oxygen consumption
    - Activity
- Scales
  - CRIES, NIPS, FLACC, CHEOPS
The Neonatal Infant Pain Scale (NIPS) is a behavioral scale and can be utilized with both full-term and pre-term infants. The tool was adapted from the CHEOPS scale and uses the behaviors that nurses have described as being indicative of infant pain or distress. It is composed of six (6) indicators.

- facial expression
- cry
- breathing patterns
- arms
- legs
- state of arousal

Each behavioral indicator is scored with 0 or 1 except "cry", which has three possible descriptors therefore, being scored with a 0, 1 or 2. See the NIPS scale for the description of infant behavior in each indicator group. Infants should be observed for one minute in order to fully assess each indicator.

Total pain scores range from 0-7. The suggested interventions based upon the infant's level of pain are listed below. The difficulty with any tool that is not self-report is the ability to differentiate between pain and agitation, however, the non-pharmacological intervention may help differentiate between these two (i.e. changing the wet diaper, feeding the infant, repositioning, etc.).

<table>
<thead>
<tr>
<th>Pain Level</th>
<th>Intervention</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-2 = mild to no pain</td>
<td>None</td>
</tr>
<tr>
<td>3-4 = mild to moderate pain</td>
<td>Non-pharmacological intervention with a reassessment in 30 minutes</td>
</tr>
<tr>
<td>&gt;4 = severe pain</td>
<td>Non-pharmacological intervention and possibly a pharmacological intervention with reassessment in 30 minutes</td>
</tr>
</tbody>
</table>
Pain Assessment

- **P**
  - Provoke – causes, better, worse?

- **Q**
  - Quality – sharp, dull, stabbing, crushing

- **R**
  - Radiating – stay in one sport, move to another location

- **S**
  - Severity – scale of 1-10

- **T**
  - Time – when start, how long does it last
Step treatment strategies - WHO

- **Mild**
  - Acetaminophen
  - NSAIDs
  - ASA
  - Celecoxib

- **Moderate**
  - Same as “Mild” + a “Moderate” opioid
    - Codeine, hydrocodone, oxycodone

- **Severe**
  - Morphine, hydromorphone, fentanyl
Step Treatment - WHO

- **STEP 1**
  - Aspirin
  - Celecoxib
  - Acetaminophen
  - NSAIDs

- **STEP 2**
  - Low potency opioids

- **STEP 3**
  - High potency opioids
Opioid Receptor

- **Agonists**
  - WHO – moderate & severe pain medications

- **Antagonists**
  - Naltrexone, naloxone

- **Mixed (agonists & antagonists)**
  - Buprenorphine, nalbuphine

- **Other**
  - Meperidine, Tramadol, methadone
Neuropathic

- Anticonvulsants
  - Pregabalin, gabapentin, carbamazepine, lamotrigine
- TCA
  - Amitriptyline, nortriptyline, doxepin etc.
Mild pain

- Celecoxib – Celebrex
  - Selective inhibitor of COX-2
    - COX-2
      - Inflammation
      - Fever
      - Pain

![Diagram showing the inhibition of cyclooxygenase 2 by Celecoxib](image-url)
Celecoxib - Celebrex

- **Kinetics**
  - Distribution – large (400 L)
  - Highly protein bound – 97%
  - Metabolized – liver CyP2C9
  - Half life – 11 hrs
  - Time to peak – 3 hrs
  - Excretion – feces & urine (metabolites & unchanged drug)

- **ADRs**
  - Edema, headache, dizziness, skin rash, abd pain, diarrhea, cough, arthralgia, fever

- **Interactions**
  - Other NSAIDs, warfarin, anticoagulants, ACEI, ARBs, alcohol, ASA products

- **Pregnancy**
  - C (less than 30 weeks) D
Opioid Receptors – Pain

- Under normal circumstances

- When opioid receptors are bound - Agonist
Opioid Receptors – Pain

- Decrease in neurotransmitters
  - Glutamate
  - Acetylcholine
  - NE
  - Serotonin
  - Substance P

- When opioid receptors are bound - Agonist

Presynaptic Receptor
Types of opioid receptors

- Classic
  - Mu
  - Kappa
  - Delta
- Non-classic
  - ORL-1
Mu Receptors - agonists

- **Endogenous**
  - Endorphins

- **Exogenous**
  - Morphine

Mu receptors are found in:
- Spinal cord
- Brainstem
- Thalamus
- Cortex

Effects:
- Analgesia
- Respiratory depression
- Euphoria
- Sedation
- Decreased GI motility
- Miosis
- Physical dependence
Delta Receptors - agonists

- **Endogenous**
  - Enkephalins

- **Exogenous**
  - DPDE (used in research)

Delta receptors are found in:

- Olfactory bulb
- Cerebral cortex
- Nucleus accumbens
- Amygdala
- Pontine nucleus

Effects

- Analgesia (spinal)
- Decreased gastrointestinal motility
- Respiratory depression?
Kappa Receptors - agonists

- **Endogenous**
  - Dynorphin

- **Exogenous**
  - Ketazocine (research)

Kappa receptors are found in:

- Limbic system
- Hypothalamus
- Brainstem
- Spinal cord

Effects:

- Analgesia – Spinal
- Sedation
- Dyspnea
- Physical dependence
- Dysphoria
- Inhibit ADH release
Mu, delta, & Kappa - antagonist

- **Naloxone**
  - Mu – Greatest affinity
  - Delta – Reduced affinity
  - Kappa – Reduced affinity

**Blocks the effects of opioids but does NOT cause the opposite effects!**
Opioids - agonists

- Uses
  - Pain
    - Cancer, surgical, obstetric, trauma, kidney & gall stones, sickle cell
  - Anesthesia
  - Adjuvant
- Others
  - Dyspnea w/MI
  - Anti-diarrheal
  - Cough suppressant

- Tolerance
- Effects
  - Analgesia, sedation, euphoria, nausea, respiratory depression
  - Effects IMMUNE to tolerance
  - Miosis & CONSTIPATION
Opioid agonists

- MOA - Binds to opioid receptors in the CNS, causing inhibition of ascending pain pathways, altering the perception of and response to pain; produces generalized CNS depression

- Medication in class
  - Codeine < hydrocodone < oxycodone < morphine < hydromorphone < fentanyl
Opioids - agonists

Kinetics

- Absorption
  - Oral – well absorbed, subject to first pass effect
  - SubQ, IM, IV – well absorbed
  - Rectal – moderate absorption
  - Lipophilic forms – nasal, sublingual, & transdermal

- Half life
  - ~2 hours

- Metabolized
  - Liver

- Excreted
  - Urine – mostly metabolites
  - Decreased in renal failure, elderly, and young
Opioids - agonists

- ADRs
  - Bradycardia, dysphoria, dependence, drowsiness, constipation, dry mouth, urinary retention, tolerance,

- Interactions
  - Drugs - Alcohol, CNS depressants, MAO inhibitors
  - Conditions (CI) – Asthma, emphysema, cor pulmonale
  - Pregnancy – C, can cross the placenta, can concentrate in breast milk
Opioid – antagonists
Naloxone/naltrexone

- **MOA**
  - Pure opioid antagonist that competes and displaces opioids at opioid receptor sites
  - Naltrexone
    - Competitive antagonist at mu opioid receptor
Opioid - antagonists

- **Naloxone**
  - Used in opioid overdose (respiratory depression)
  - Not orally bioavailable (parenteral administration)
  - Half life – 30-90 minutes
  - Duration – 1-2 hours

- **Naltrexone**
  - Differences
  - Orally bioavailable (PO & IM)
  - Higher potency
  - Half life – 3 hours
  - Duration – 24-28 hours
  - Active metabolite (13 hours)
Opioids – mixed agonist/antagonists

- **Benefits**
  - Pain relief w/o as many addictive qualities
  - Less respiratory depression & constipation

- **Risks**
  - Can cause withdrawal symptoms (not for opioid dependent patients)

- **Types**
  - Buprenorphine, nalbuphine, others
Others

- **Tramadol**
  - **MOA** – Binds to μ-opiate receptors in the CNS causing inhibition of ascending pain pathways, altering the perception of and response to pain; also inhibits the reuptake of norepinephrine and serotonin, which are neurotransmitters involved in the descending inhibitory pain pathway responsible for pain relief.
Tramadol

- **Kinetics**
  - Onset – 1 hour
  - Duration – 9 hrs
  - Absorption – rapid & complete
  - Metabolism – liver
  - Half life
    - Parent – 6-8 hrs
    - Metabolite – 7-9 hrs
  - Excretion - urine

- **ADRs** – Similar to opioid agonists
  - CNS – dizziness, stimulation, headache, insomnia
  - Constipation, N&V
  - Weakness

- **Interactions** – MAO inhibitors, alcohol, CNS depressants

- **Pregnancy** – C
## Others

- **Meperidine**
  - Used - Surgery
  - Phenylpiperidine – still binds mu receptor
  - Not cough suppressant or antidiarrheal
  - Can accumulate and cause SEIZURES
  - Interaction – MAO inhibitors
  - ADRs – hyperthermia, muscle twitching, hallucinations

- **Methadone**
  - Used - addiction
  - Phenylheptylamines – binds to mu receptor
  - Inhibits NMDA & re-uptake of catecholamines/serotonin
  - Substances added to tablets to prevent abuse
  - Variable kinetics
    - Bioavailability – 36-100%
    - Half life – 8-59 hrs
    - Metabolized by CYP3A4 & 2B6
    - Can prolong QTc interval (EKG)
Tricyclic Antidepressants

- MOA - Increases the synaptic concentration of serotonin and/or norepinephrine in the central nervous system by inhibition of their reuptake by the presynaptic neuronal membrane pump
- Various types of pain (neuropathic pain) – off label
- Emotional aspect of pain
- Amitriptyline, nortriptyline, doxepin, imipramine
Tricyclic Antidepressants

- **Kinetics**
  - Onset: 4-8 weeks
  - Absorption: rapid
  - Metabolism: liver
  - Half life: 13-36 hours
  - Excretion: urine
  - Can accumulate in elderly

- **ADRs**
  - Anticholinergic, decrease blood pressure, sedation, EPS

- **Interactions**
  - Anticholinergic agents, BP agents, CNS depressants

- **Pregnancy – Risk C**
Anticonvulsants

- MOA – Vary with individual agents
  - Generally all have CNS effects involving neurotransmitters
- Calm the over-activity/excitability of the CNS
- Types
  - Gabapentin, pregabalin, lamotrigine, carbamazepine....
Anticonvulsants

- Best for neuropathic pain
- Select based on adverse drug effect profiles
- Drug-drug interactions
  - Carbamazepine – MAJOR CYP enzyme inducer
- Select based on ease of treatment
  - Dosing schedule
Questions