Acute Pain Management in the Hospital Setting

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What is Pain?

- “An unpleasant sensory and emotional experience associated with actual or potential tissue damage or described in terms of such damage”
- “Whatever the patient says it is”

Epidemiology

- ~25 million experience acute pain from injury or surgery/year
- ~80% of patients experience post-operative pain
  - <50% report adequate pain relief
  - 10-50% will develop chronic pain
  - 2-10% have severe chronic pain
- Pain is the most common symptom experienced by patients in the hospital

Significance

Inadequate acute pain treatment

- Chronic pain
- Prolonged rehabilitation
- Reduction in quality of life
- Negative social/psychological effects

Appropriate pain management

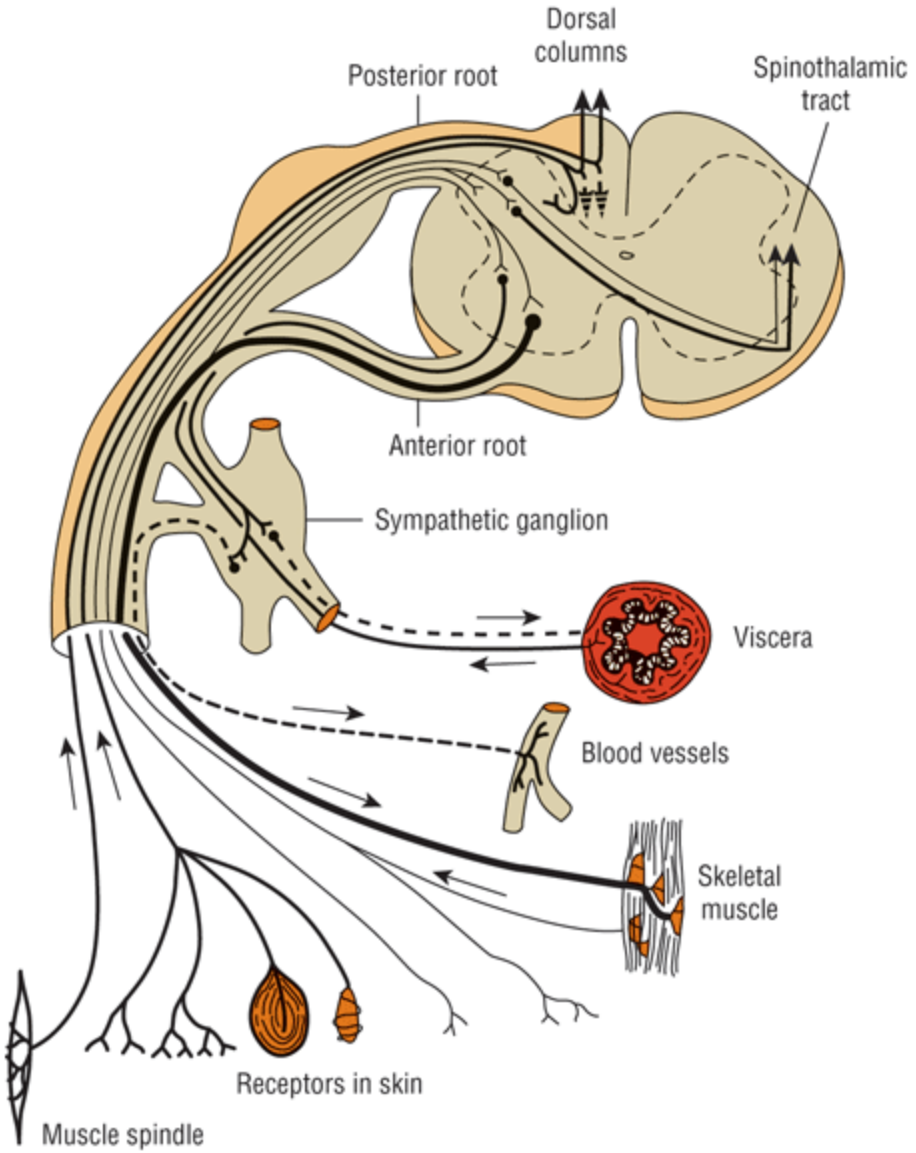
- Reduction in hospital length of stay and costs
- Increase patient satisfaction

Patient Case: Maria, 65 yo F

- CC:
  - Increasing abdominal pain
- PMH:
  - Stage 3 colon cancer, CKD Stage 3, seizure hx
- Drug allergies:
  - Morphine
- Home pain regimen:
  - Oxycodone/acetaminophen 10-325 mg q6h
- Inpatient pain regimen: Pain score 7/10
  - Oxycodone/acetaminophen 10-325 mg q6h
  - Acetaminophen 650 mg PO q4h prn mild pain (x0 doses)
  - Morphine 2 mg IV q4h prn mod-severe pain (x6 doses)

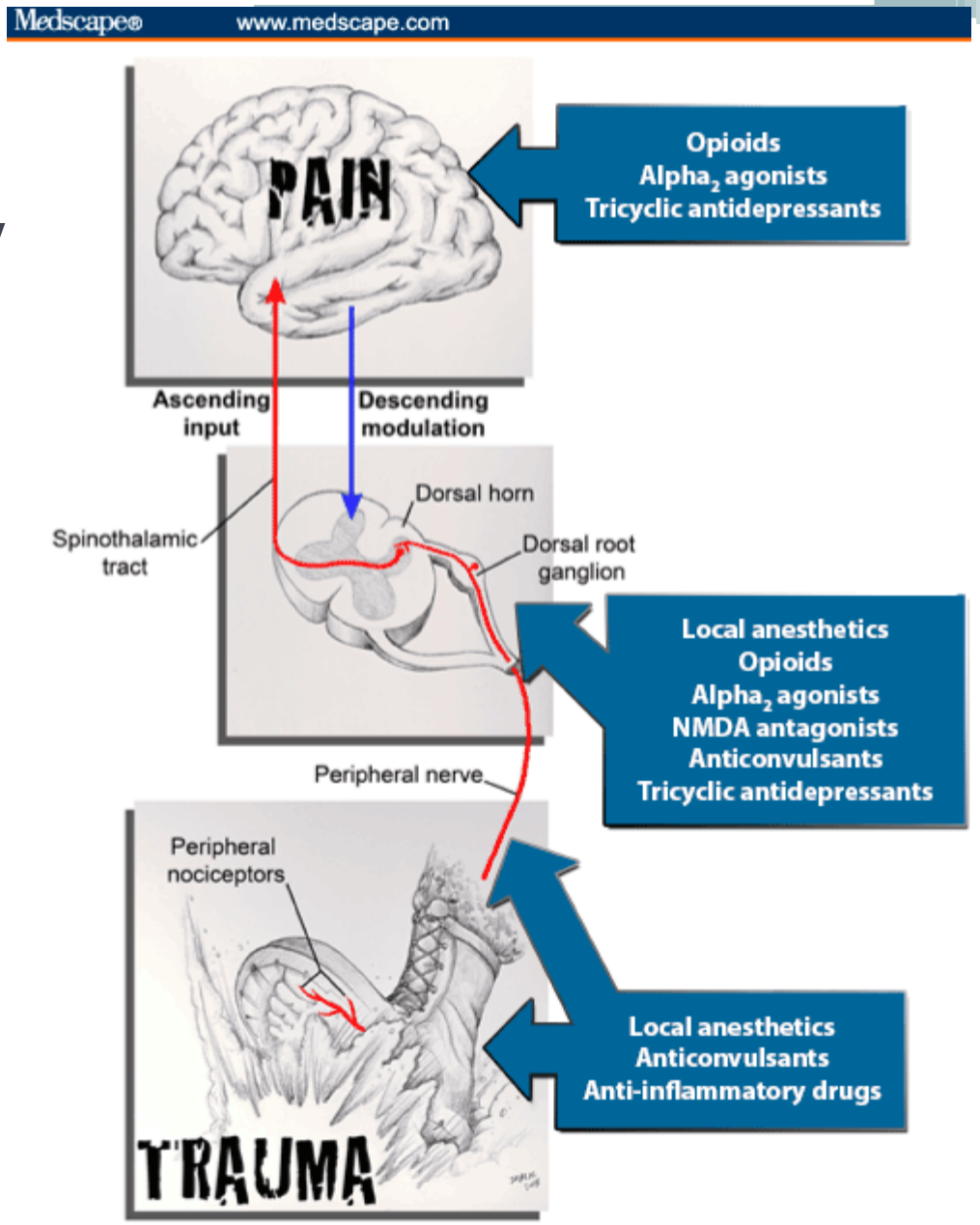
Types of Pain

- Acute vs. chronic
- Musculoskeletal
- Nociceptive
  - Somatic
  - Visceral
- Neuropathic
- Inflammatory



Pathophysiology

- Stimulation
- Transmission
- Modulation
- Perception



Tolerance, Physical Dependence, Addiction, Pseudoaddiction

Tolerance

- Diminishing of drug effect over time as a consequence of exposure to the drug

Physical dependence

- The occurrence of an abstinence syndrome following administration of an antagonist drug or abrupt dose reduction or discontinuation

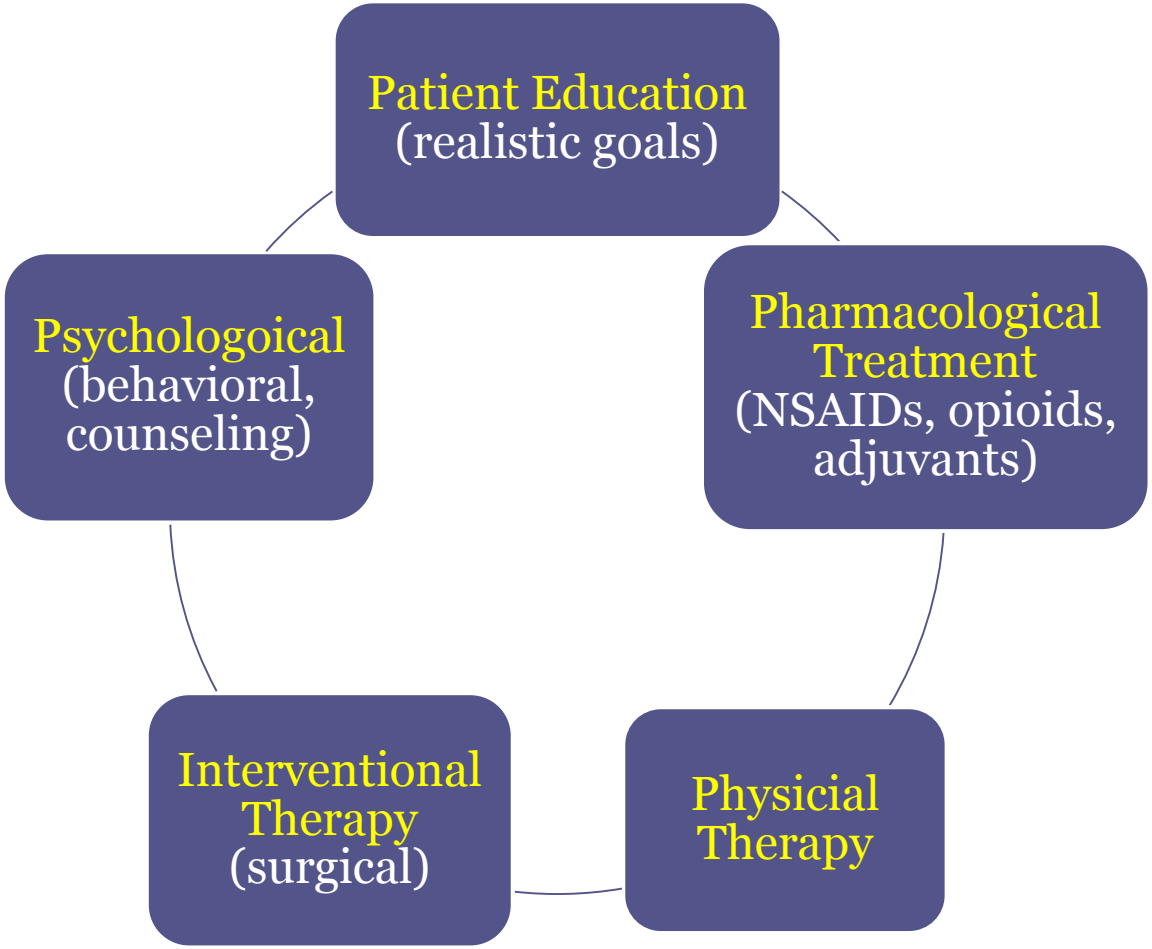
Addiction

- A behavioral pattern characterized by loss of control over drug use, compulsive drug use, and continued use of a drug despite harm

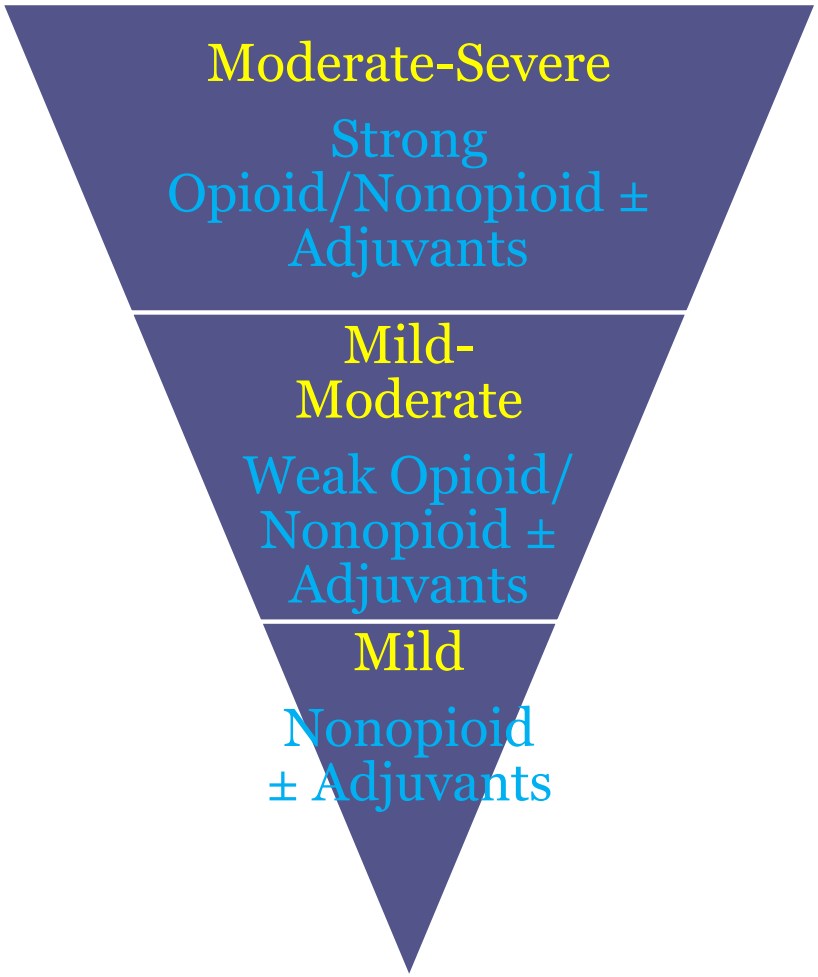
Pseudoaddiction

- Behavior that may suggest addiction, but is actually a reflection of unrelieved pain

Multimodal Approach



WHO 3-Step Pain Ladder



- Nonopioid analgesics:
  - Acetaminophen
  - NSAIDs
  - Aspirin
  - Salicylates
- Weak opioids:
  - Codeine
  - Hydrocodone
  - Tramadol
- Strong opioids:
  - Morphine*
  - Hydromorphone*
  - Fentanyl
  - Methadone
  - Oxycodone*
  - (*can be used for mild-moderate pain at low doses)

Patient Assessment

Description of pain

What relieves the pain?

What causes or increases pain?

Effects of pain on physical, emotional, and psychological function

Patient's pain and functional goals

True Allergy vs. Pseudoallergy

Classifications of Opioids

Phenanthrenes	Phenylpiperidine	Phenylheptane
• Morphine • Codeine • Hydromorphone • Oxycodone • Hydrocodone	• Meperidine • Fentanyl	• Methadone

- ➢Switch to another opioid class (low cross sensitivity)
- ➢Switch to a higher potency opioid

Opioid-Naïve vs. Opioid-Tolerant

- Opioid-tolerant patient: Use of the following for **at least 7 days or longer** -
  - 60 mg oral morphine/day
  - 25 mcg transdermal fentanyl/hr
  - 30 mg oral oxycodone/day
  - 8 mg oral hydromorphone/day
  - 25 mg oral oxymorphone/day
  - An equianalgesic dose of another opioid

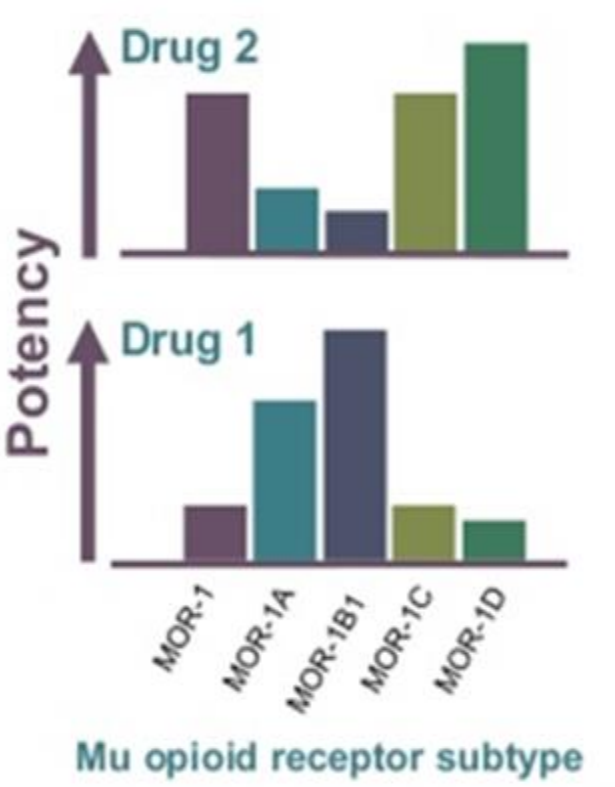
Opioid Naïve: Dose Initiation

- Acute, severe pain:
  - Morphine
    - 2-5 mg IV q4h PRN
    - Elderly – start low, go slow
  - Hydromorphone
    - 0.5-1 mg IV q4h PRN
  - Oxycodone
    - 2.5-7.5 mg q4h PRN

Scheduled Regimens

- Chronic pain:
  - Long-acting opioid + short-acting opioid
- Breakthrough pain
  - 10% of total daily dose (24-hr) -> every hr PRN

Incomplete Cross-Tolerance



Mu opioids bind to mu receptors

Many mu receptor subtypes:

- Mu opioids produce subtle differences in pharmacological response based on activation profiles of mu receptor sybtypes

Explains:

- Inter-patient variability in response to mu opioids
- Incomplete cross-tolerance among mu opioids
- Importance of calculating % dose reductions when switching opioids

Opioid Rotation

Calculate equianalgesic dose of new opioid

Reduce equianalgesic dose by 25-50%*

*75-90% reduction for methadone

Current opioid regimen	Current pain control	Elderly/ medically frail	Same drug, different route

Equianalgesic Opioid Dosing

Drug	Parenteral (mg)	Oral (mg)
Morphine	10	30
Hydromorphone	1.5	7.5
Oxycodone	N/A	20
Oxymorphone	1	10
Hydrocodone	N/A	30
Codeine	130	200
Meperidine	75	300
Fentanyl	0.1	N/A

Hepatic Impairment: Opioid Metabolism

Opioid	Extraction Ratio
Codeine	0.52
Fentanyl	0.80-1.0
Hydromorphone	0.51
Methadone	<0.30
Meperidine	0.52
Morphine	0.76
Pentazocine	0.80

Metabolism	Opioid Affected
CYP3A4 (Phase 1)	Fentanyl, oxycodone, tramadol
CYP2D6 (Phase 1)	Codeine, hydrocodone
Glucuronidation (Phase II)	Hydromorphone, oxymorphone, morphine

Hepatic Impairment: Recommendations

Opioid	Recommendation
Codeine	**Not recommended;** prodrug, reduced conversion to active metabolite -> poor analgesic effect
Fentanyl	99% metabolized in liver; careful monitoring
Hydrocodone	Use with caution; monitor for overdose due to reduced metabolism of parent compoound
Hydromorphone	Use with caution; undergoes phase II reaction and intermediate extraction ratio
Methadone	Use with caution; risk of accumulation due to increased free drug
Meperidine	**Not recommended;** toxic metabolite, normeperidine, may accumulate
Morphine	Use with caution; monitor for overdose due to high extraction ratio
Oxycodone	Use with caution; reduce dose by 25-50%
Oxymorphone	**Contraindicated** in moderate-severe hepatic impairment
Tramadol	**Not recommended**

Renal Impairment: Dosing

% Dose Reduction

GFR (mL/min)	Morphine	Hydromorphone	Oxycodone	Methadone	Fentanyl
>50	N/A	0-50%	N/A	N/A	N/A
10-50	50-75%	50%	50%	N/A	0-25%
<10	Not recommended	25%	Not recommended	0-25%	50%

Renal Impairment: Recommendations

Opioid	Recommendation
Codeine	Not recommended due to accumulation
Fentanyl	Appears safe; adjust dose if needed
Hydrocodone/oxycodone	Use with caution; adjust dose if needed
Hydromorphone	Use with caution; adjust dose if needed
Methadone	Appears safe; adjust dose if needed
Meperidine	Not recommended due to metabolites
Morphine	Not recommended due to metabolites
Tramadol	Not recommended

Management of Adverse Effects

Pruritis	• Non-IgE mediated mast cell binding and histamine release • Antihistamines, anticholinergics
N/V	• Stimulation of chemoreceptor trigger zone (CTZ) • Antipsychotics, metoclopramide, serotonin antagonists
Constipation	• Stimulates mu receptors in GI tract causing slowed GI motility • Scheduled prophylaxis bowel regimen (doc/senna, PEG, fluids, fiber)
Respiratory depression	• Caution in patients with chronic lung disease (COPD, asthma) • Incidence is very low and associated with overdose
Sedation	• CNS depressants (benzodiazepines, alcohol use) • Stimulants (methylphenidate)

Medication Pearls

Acetaminophen

- Analgesic effects only (not anti-inflammatory)
- Maximum dose <4g/day
- Alcohol use increases risk for hepatic toxicity
- Oral – onset <1 hr
- Rectal – slow, unpredictable absorption
- IV – $$$

NSAIDs

- Use:
  - Mild-moderate-severe pain, cancer-related bone pain
- Avoid combining NSAIDs (additive toxicities)
- Increase to maximum dose → change if ineffective
- Ketorolac:
  - IV/IM; short term use only (max = 5 days)
- Add GI prophylaxis:
  - Assess CVD risk vs. GI bleed risk
- A/E: renal toxicity
  - D/c NSAID if BUN or Cr doubles

Adjuvant Analgesics

- Use
  - Chronic pain (inflammatory, neuropathic)
- Anticonvulsants
  - Decrease neuronal excitability
- TCAs and SNRIs
  - Enhance pain inhibition
- Topical anesthetics
  - Decrease nerve stimulation

Codeine

- Commonly used combined
  - Mild-mod pain
- FDA BW:
  - Risk of death in CYP450-2D6 rapid metabolizers
- Poor analgesic potency
- A/E:
  - Increased nausea and constipation
- Active metabolite:
  - Morphine

Hydrocodone

- Commonly used in combination
- A/E
  - Nausea, constipation (less than codeine)
- Reduce dose in severe hepatic impairment
- Metabolites accumulate in renal insufficiency

Tramadol

- MOA
  - Binds to mu-opioid receptors
  - Inhibits serotonin and norepinephrine reuptake
- Use
  - Mod-severe pain
  - Chronic pain, neuropathic pain
- A/E
  - N/V
- Serotonin syndrome and seizure risk - (max 400 mg/day)
  - Use with other drugs that reduce seizure threshold
  - Hx of seizures
  - Reduce dose in renal impairment and elderly

Morphine

- Gold standard for conversions
- Drug of choice
  - Severe pain, ACS pain (decrease in myocardial oxygen demand)
- Multiple dosage forms
  - PO, IV/IM/SC, Spinal IT, epidural, SL, rectal
- A/E
  - Orthostatic hypotension, pruritis
- Renal impairment
  - M3G metabolite accumulates in renal impairment → neurotoxicity, seizures
- Hepatic impairment
  - Lengthen frequency in administration

Oxycodone

- Useful
  - Moderate-severe pain
  - IR or ER for acute or persistent pain
  - Available in combination
- >potent than morphine
- PO only

Hydromorphone

- Compared to morphine
  - >Potent than morphine
  - Better oral absorption
  - Similar pharmacological profile
- Renal impairment
  - Toxic metabolite hydromorphone-3-glucuronide (H3G)

Oxymorphone

- > potent than morphine, oxycodone
- Available in
  - PO, rectal, IV
- Poor oral bioavailability (~10%)
- Administration
  - Take on empty stomach
- Good option for patients complaining of pruritis reaction from morphine
  - Higher potency and reduced histamine release

Fentanyl

- High potency, short acting
  - 10 mg morphine IV q4h ~ 100 mcg fentanyl IV q1h
- Avoid
  - Opioid naïve patients
- Useful
  - Around the clock pain, bowel obstruction, severe opioid-induced constipation or pruritis
- Available
  - Patch - 72h duration, chronic pain use only
    - 12-24 hrs for full onset, up to 6 days to reach steady state
    - Good alternative for pts on stable regimens
  - IV, IT, SL

Methadone

- Pearls
  - Oral efficacy, extended duration of action, low cost
  - Prolongs QT – risk of torsades de pointes
  - Unpredictable half life, possible excessive sedation, difficulty in titration
- MOA:
  - Mu and Kappa opioid agonist effects
  - NMDA antagonist
  - SNRI
- Useful
  - Neuropathic and chronic pain
  - Poor pain control with opioids
  - Renal dysfunction (no active metabolites)
  - Less constipating
- Available
  - PO, IV, IM, SL

Meperidine

- Neurotoxicity, seizures = Max (300 mg/day IV)
  - Higher risk in elderly or renal impairment – accumulation of toxic metabolite, normeperidine
- Weak analgesic effect ~ 10-fold < potent than morphine
  - Short duration of action - more frequent and higher doses for pain relief
- Not recommended for long term use

Buprenorphine

- Indication: treatment for opioid dependency

Naloxone

- MOA
  - Pure opioid antagonist
  - Binds competitively to opioid receptors w/o analgesic effects
- Use
  - Opioid reversal agent
- Dose
  - 0.04 – 0.4 mg

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Patient Case: Maria, 65 yo F

- What are some patient-specific considerations?
- What are her preferred treatment options?
- What is your recommendation?
- When to consider a long-acting agent?

Patient Case: Maria, 65 yo F

- Patient specific factors
  - Age, hepatic and renal impairment, hx of seizures, morphine allergy, opioid-tolerant
- Preferred treatment options?
  - Switching morphine -> hydromorphone
  - Switching to fentanyl
  - Increasing oxycodone-apap dose
- Not recommended
  - Meperidine and tramadol (hx of seizures, renal impairment)
- When to consider a long-acting agent?
  - If patient has a chronic pain condition
  - Had ~3 or more prn doses for severe pain

Questions?

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