Non-opioid and adjuvant pain management

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Disclosures

- I have no financial disclosures*

My Background

- MD with Distinction in Research
- Internal Medicine & Psychiatry board certified
- Hospice & Palliative Medicine board certified
- Certificate in Medical Education
Objectives

- Review principles of pain management
- Review adjuvant analgesics
  - Inflammatory pain
  - Neuropathic pain
  - Bone pain
  - Bowel Obstruction

Patient Case: Mr. P

- 60 yo man with history of anxiety, chronic pain
- New diagnosis of malignancy of unknown primary
- “Stage II” sacral decubitus ulcer
- Failed ketamine trial at hospital
- Methadone 50mg q6h scheduled
- Valium 10mg TID
- Started on Fentanyl 50mcg q15 min PCA by weekend physician
- Hurting “everywhere”
- Goal is to die at home

General approach to pain management

- Detailed pain history
- Physical exam
- Associated factors
Adjuvant Analgesics

- Primary indication other than pain
- Can be used alone or in combination with analgesics
- Often used with opioids to enhance pain relief, treat pain that is refractory to opioids, or as an “opioid-sparing” agent
- Commonly used for pain syndromes

Inflammatory Pain Analgesics

- NSAIDS
  - Inhibit COX-1 and COX-2
  - Inhibit prostaglandin synthesis
  - Administered orally, rectally, topically, intravenously, and intramuscularly
- Aspirin
  - Irreversibly inhibits COX-1 and COX-2
  - COX-1 inhibition can affect gastrointestinal tract, kidneys, central nervous system, platelet function
Inflammatory Pain Analgesics

- NSAIDs are considered first line treatment for non-cancer pain
- Inflammatory joint disease
- Myalgias
- Back pain
- Headaches
- Surgical pain

Inflammatory Pain Analgesics

- NSAIDs are helpful in cancer related pain
- Bone pain – due to distention of the periosteum by metastases
- Soft tissue pain – due to compression or distention of tissues
- Visceral pain – due to irritation of the pleura or peritoneum

Adjuvant Analgesics - Corticosteroids

- Dexamethasone commonly used
- Works by inhibiting arachidonic acid cascade to reduce inflammation
- Improves appetite, nausea, malaise, and quality of life
- Multiple indications
- Multiple side effects
**Adjuvant Analgesics - Paracetamol**

- Also known as acetaminophen
- Mechanism of action is poorly understood
- Administered orally, rectally, and intravenously
- Used alone or with opioids
- Toxicity can occur with doses greater than 4g/day

**Adjuvant Analgesics for Neuropathic Pain**

- Tricyclic antidepressants (amitriptyline, nortriptyline, doxepin, etc.)
- Used for fibromyalgia, spinal cord injury pain, cancer-related pain, depression, post-herpetic neuralgia
- Side effects include cardiotoxicity, orthostatic hypotension, somnolence, and anticholinergic effects
- Use lower dose if combining with a selective serotonin reuptake inhibitor
Adjuvant Analgesics for Neuropathic Pain

- Noradrenaline and serotonin reuptake inhibitors (venlafaxine, duloxetine, etc.)
- Used for atypical facial pain, fibromyalgia, and chronic post-mastectomy pain
- Side effects include nausea, headache, hypertension, sedation, insomnia, weight gain, and sexual dysfunction
- Use lower dose of venlafaxine in patients with hepatic and renal impairment

Putting it all Together

<table>
<thead>
<tr>
<th>Class</th>
<th>Drug (Brand)</th>
<th>Indication</th>
<th>Dosing Range</th>
<th>Sedation</th>
<th>ACH</th>
<th>Insomnia</th>
<th>Orthostasis</th>
<th>GI</th>
<th>Weight gain</th>
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<tbody>
<tr>
<td>TCA</td>
<td>Amitriptyline (Elavil)</td>
<td>Fibromyalgia, Spinal cord injury pain, Cancer-related pain, Post-herpetic neuralgia</td>
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<td>Nortriptyline (Aventyl, Pamelor)</td>
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<td>Doxepin (Sinequan, Adapin)</td>
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Adjuvant Analgesics for Neuropathic Pain

- Carbamazepine
- Trigeminal neuralgia, post-herpetic neuralgia, and diabetic neuropathy
- Use limited by side effects: leukocytosis, thrombocytopenia, dizziness, drowsiness, ataxia, nausea, vomiting, blurred vision, agranulocytosis, aplastic anemia, and Stevens-Johnson syndrome
- Obtain laboratory tests before and during treatment
Adjuvant Analgesics for Neuropathic Pain

- Gabapentin and pregabalin
  - Considered first line agents for treatment of non-malignant neuropathic pain
  - Side effects: Drowsiness, edema, weight gain, and dizziness
  - Maximum dose of gabapentin: 3600mg/day
  - Adjust for renal dysfunction

- Lamotrigine
  - Trigeminal neuralgia, HIV neuropathy, and central post-stroke pain
  - Most common side effect is an exfoliative rash
  - Usual effective dose is between 200-500mg/day

Putting it all Together Again

<table>
<thead>
<tr>
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<th>Insomnia</th>
<th>Orthostasis</th>
<th>GI</th>
<th>Weight Gain</th>
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<td>Pregabalin (Lyrica)</td>
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<tr>
<td>Lamotrigine (Lamictal)</td>
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<td>200-500mg</td>
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<td>+++</td>
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Adjuvant Analgesics for Neuropathic Pain

- Lidocaine
  - Works by blocking sodium channels
  - IV route not shown to be effective in clinical trials
  - Clinical experience may justify IV use for refractory neuropathic pain
  - Contraindicated for patient with cardiac conduction disorders and seizure disorders
  - Topical route well tolerated

- Ketamine
  - Analgesic doses lower than anesthetic doses
  - Antagonist at the N-methyl-D-aspartate receptor
  - Also acts at many other receptors: such µ-opioid, muscarinic, monoaminergic, gammaaminobutyric receptors, etc.
  - Intravenous, oral, rectal, subcutaneous, and topical routes
  - Toxicities
    - Neuropsychiatric: dysphoria, hallucinations, nightmares
    - Cardiovascular: tachycardia, hypertension
Adjuvant Analgesics for Neuropathic Pain

- Alpha-2 adrenergic agonists (clonidine, tizanidine)
- Chronic headache, non-malignant neuropathic pain, and some neuropathic cancer-related pain
- Oral or transdermal route
- Mechanism of analgesia is unknown
- Side effects include somnolence, hypotension, and dry mouth

Adjuvant Analgesics for Bone Pain

- Calcitonin and bisphosphonates
- Bone metastases and vertebral compression fractures
- Inhibit osteoclast activity
- Subcutaneous or intranasal route
- Side effects include renal toxicity, gastrointestinal toxicity, and osteonecrosis of the jaw
- Use with caution in patients with renal and hepatic impairment
Adjuvant Analgesics for Bone Pain

- Radiopharmaceuticals
- Absorbed at areas of high bone turnover
- Strontium-89, Samarium-153
- Given as monotherapy or with radiation therapy
- Main side effect – myelosuppression
- Radiation therapy alone

Adjuvant Analgesics for Bowel Obstruction

- Octreotide
  - Inhibits the secretion of gastric, pancreatic and intestinal secretions
  - Reduces gastrointestinal motility
  - Corticosteroids

Back to Mr. P

- Final regimen:
  - Methadone 60mg oral concentrate po q6h scheduled
  - Fentanyl 500mcg/hr continuous infusion
  - Fentanyl 500mcg q10min PCA
  - Toradol 30mg IV q6h scheduled
  - Dexamethasone 10mg IV daily
  - Ativan 2mg IV q8h scheduled
  - Trapeze bar for bed
  - Taught wife how to administer IV medications and wound care
  - Patient returned home
Summary

- Start with history and physical exam to select appropriate adjuvant therapy
- Start low, go slow
- Monitor for side effects
- Can be used alone or with opioid therapy for patients with complex pain syndromes

Questions?