A Pain Management Primer for Pharmacists

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Objectives

• Discuss the differences between somatic, visceral, and neuropathic pain
• Design a treatment plan for the different modalities of pain
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What is Pain?

“An unpleasant sensory and emotional response associated with actual or potential tissue damage or described in terms of such damage.” (IASP)


What is Pain?

“Pain is whatever the person says it is”
-Margo McCaffery
Types

Acute vs Chronic

Nociceptive vs Neuropathic vs Mixed

Associated Syndromes

Hyperalgesia
• Increased pain sensitivity to a normally noxious stimulus

Allodynia
• Pain in response to a stimulus which is normally not noxious
  • i.e. blankets, clothing
Nociception

Activation of peripheral nerve receptors by a noxious stimulus

Mechanical
• Pressure
• Stretch

Thermal

Chemical
Total Pain

- Physical Symptoms
- Emotional Psychological Problems
- Social Concerns
- Spiritual Existential Distress

Patient with Pain
How Pain Works

1. Transduction

2. Conduction

3. Transmission

4. Perception

Modulation happens all along the way
How Pain Works

Transduction
• Conversion of mechanical or chemical stimuli into an electric charge

Conduction
• Impulses from primary nociceptors to the spinal cord

Transmission
• Transmitting nociceptive impulses from the dorsal horn to supra-spinal targets

Perception
• Subjective awareness of pain

Modulation
• Reduction of transmission
## How Pain Works

### Excitatory Neurotransmitters
- Substance P
- Substance K
- Glutamate
- Aspartate
- Calcitonin gene related peptide
- Vasoactive intestinal peptide

### Inhibitory Neurotransmitters
- Serotonin
- Norepinephrine
- Opioids
- GABA
- Somatostatin
- Galanin
Nociceptive Pain

Somatic Pain
Skin, soft tissue, bone
• Easy to describe, localize

Visceral Pain
Organs
• Difficult to describe, localize

Described as...
Sharp
Aching
Throbbing
Neuropathic Pain

Nervous System Damage

- Primary lesion
- Dysfunction

Pain may be greater than observable injury

Described as:
- Burning
- Electrical
- Shooting
- Stabbing
- Tingling

Assessment

Precipitating and palliating factors, previous tx
Quality
Region and radiation
Severity
Temporal profile
(you)
  • How does the pain affect the patient
Patient Case

MC is a 56 y.o. male with metastatic NSCLC with new bone metastasis, uncontrolled DM2, and HTN

• Reports continuous 8/10 generalized pain and 10/10 pain in his L hip which he reports is negatively affecting his ability to take care of his family
• Described “sharp, aching, throbbing pain in his L hip”, feels as if his feet “are always on fire”

Current Pain Medications:
Oxycodone ER 120 mg PO TID
Oxycodone 80 mg PO Q3H prn
Gabapentin 300 mg PO TID
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Treatment Options
Treatment options

**Transduction** – anti-inflammatories, local anesthetics

**Conduction** – opioids

**Transmission** – NMDA receptor antagonists, gabapentinoids, anti-epileptics, opioids, lidocaine/mexilitine

**Perception** – NO DRUGS!
- THC may play a role here
- Cognitive behavioral therapy

**Modulation** – enhancing descending inhibitory pathway (opioids, TCAs, SNRIs, etc.)
**Mechanism-Specific Treatment**

Multiple targets...

- **Peripheral Sensitization** (Na⁺ channels)
  - NSAIDs
  - Opioids
  - TCA
  - Lidocaine

- **Spinal Cord**
  - NSAIDs
  - Opioids
  - TCA
  - Gabapentin
  - Lidocaine

- **Descending Inhibition** (NE, 5HT)
  - TCA
  - SNRI
  - Tramadol
  - Opioids

- **Central Sensitization** (Ca²⁺ channels, NMDA receptors)
  - TCA
  - SNRI
  - Tramadol
  - Opioids

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**Rational Polypharmacy**
Medications Affecting Transduction

Non-steroidal anti-inflammatories (NSAIDs)

Local anesthetics
  topical lidocaine
## Medications Affecting Conduction

### Opioids

<table>
<thead>
<tr>
<th>Full Mu Agonists</th>
<th>Partial Mu Agonists</th>
<th>Agonist/Antagonist</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oxycodone</td>
<td>Hydrocodone</td>
<td>Buprenorphine</td>
</tr>
<tr>
<td>Codeine</td>
<td>Morphine</td>
<td>Pentazocine</td>
</tr>
<tr>
<td>Hydromorphone</td>
<td>Fentanyl</td>
<td>Butorphanol</td>
</tr>
<tr>
<td>Meperidine</td>
<td>Tramadol*</td>
<td>Nalbuphine</td>
</tr>
<tr>
<td>Tapentadol*</td>
<td>Methadone**</td>
<td></td>
</tr>
</tbody>
</table>
# Opioid Receptors

<table>
<thead>
<tr>
<th>Opioid Receptor Class</th>
<th>Analgesic Effects</th>
<th>Adverse Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mu₁</td>
<td>Supraspinal analgesia</td>
<td>Euphoria, confusion, dizziness, nausea, low addiction potential</td>
</tr>
<tr>
<td>Mu₂</td>
<td>Spinal analgesia</td>
<td>Respiratory depression, cardiovascular and GI effects, miosis, urinary retention</td>
</tr>
<tr>
<td>Delta</td>
<td>Spinal analgesia</td>
<td>Cardiovascular depression, decreased brain and myocardial oxygen demand</td>
</tr>
<tr>
<td>Kappa</td>
<td>Spinal analgesia</td>
<td>Dysphoria, psychomimetic effects, feedback inhibition of endorphin system</td>
</tr>
</tbody>
</table>
Opioids

Important to understand potency differences
Fentanyl > hydromorphone > oxycodone > morphine/hydrocodone > codeine

Side Effect Profile
- Nausea
- Vomiting
- Constipation
- Confusion
- Respiratory depression
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Medications Affecting Transmission

• NMDA antagonists
  • Methadone
  • Ketamine

• Anticonvulsants
  • Sodium Channel Blockers
  • Calcium Channel Blockers

• Lidocaine/mexilitine

• Opioids
NMDA Antagonists

Methadone
  Unique pharmacokinetic profile
  Neuropathic or mixed pain
  Hyperalgesia/allodynia

Ketamine
  Can decrease opioid requirement
  Neuropathic or mixed pain
  Hyperalgesia/allodynia
# Anticonvulsants

<table>
<thead>
<tr>
<th>Medication</th>
<th>Recommended Starting Dose</th>
<th>Common Side Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gabapentin</td>
<td>100-300mg QHS</td>
<td>Drowsiness, dizziness, edema, fatigue</td>
</tr>
<tr>
<td>Pregabalin</td>
<td>25mg q12H</td>
<td></td>
</tr>
<tr>
<td>Topiramate</td>
<td>200mg Q12H</td>
<td>Weight loss, agitation, kidney stones, glaucoma</td>
</tr>
<tr>
<td>Cabamazepine</td>
<td>50mg q12H</td>
<td>Skin reactions, hepatotoxicity, hyponatremia, CNS depression</td>
</tr>
<tr>
<td>Valproic Acid</td>
<td>125-250mg BID or Q8H</td>
<td>Drowsiness, dizziness, nausea, thrombocytopenia, flu-like symptoms, tremor</td>
</tr>
</tbody>
</table>
Lidocaine/mexilitine

Sodium channel blockade
If lidocaine is tolerated, can switch to oral mexilitine
Medications Affecting Modulation

Tri-cyclic antidepressants (TCA)
Serotonin and norepinephrine re-uptake inhibitor (SNRI)
Opioids
<table>
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<tr>
<th>Medication</th>
<th>Recommended starting dose</th>
<th>Common Side Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amitriptyline</td>
<td>10mg QHS</td>
<td>Anticholinergic, sedation, QT prolongation</td>
</tr>
<tr>
<td>Nortriptyline</td>
<td>10mg QHS</td>
<td>Anticholinergic, QT prolongation, sexual dysfunction</td>
</tr>
</tbody>
</table>
## SNRI

<table>
<thead>
<tr>
<th>Medication</th>
<th>Recommended starting dose</th>
<th>Common Side Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Venlafaxine</td>
<td>37.5mg daily</td>
<td>Nausea. Insomnia or drowsiness</td>
</tr>
<tr>
<td>Duloxetine</td>
<td>60mg daily</td>
<td>Headache, drowsiness, fatigue, nausea</td>
</tr>
</tbody>
</table>
Effects of Untreated Pain

Untreated pain can...
- Alter neurotransmission signals
- Modulate pain pathways
- Make it more difficult to treat pain in the future
- Lead to chronic pain condition

Other effects include...
- Endocrine/metabolic, respiratory, musculoskeletal, gastrointestinal and immunologic
## Barriers

<table>
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<tr>
<th>Practice Issue Barrier</th>
<th>Potential Problems</th>
</tr>
</thead>
<tbody>
<tr>
<td>Failure to use more than medications</td>
<td>Miss benefits of physical, behavioral and psychological therapies to help re-train the central nervous system</td>
</tr>
<tr>
<td>Failure to target mechanism of pain</td>
<td>Under-treated pain</td>
</tr>
</tbody>
</table>
| Failure to treat neuropathic pain with adjuvants | Increased nervous system hypersensitivity  
Under-treated pain                                                                 |
| Reliance on short acting opioids             | Increased breakthrough, disturbed sleep  
Opioid tolerance                                                                 |
References

19. www.med.ohio.gov