Pain Management in Primary Care

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Pain in Primary Care

• Pain was primary reason for 40% of doctor visits in a Finnish study from 2001
  ✓ Most common reason for visiting doctor
• Not enough pain specialists to treat all the patients with chronic pain
• Primary care doctors will end up managing most pain problems
• Easier if some basic principles in mind

Pain Definition

• Pain is an unpleasant sensory and emotional experience associated with actual or potential tissue damage or described in terms of such damage
• Pain is always subjective

Pain Mechanisms

• Traditional pain categories:
  ✓ Nociceptive
    • Somatic
    • Visceral
  ✓ Neuropathic
  ✓ Complex Regional Pain Syndrome (CRPS)
    • Formerly Reflex Sympathetic Dystrophy (RSD)
### Acute vs. Chronic Pain

- **Acute pain**
  - Well-defined, temporal pattern of onset
  - Associated with subjective and objective physical signs and with hyperactivity of the autonomic nervous system
  - Usually self-limited
  - Responds to analgesic treatment and/or treatment of underlying disease

- **Chronic pain**
  - Pain that lasts for longer than 3-6 months
  - Or longer than normal healing process
  - Nervous system dysregulation results in hypersensitivity to pain
    - Spontaneous generation & perpetuation of pain
    - Adaptation of the autonomic nervous system
    - Lack of objective signs and symptoms
  - Pain becomes a problem in itself
  - Changes in personality, lifestyle, & function

### Chronic Malignant Pain vs. Chronic Non-malignant Pain

- **Pathophysiology is similar**
- **Difference in longevity may be important**
- **Malignant pain associated with diminishing function due to disease progression**
- **Risks of long-term opiate therapy may be more significant in benign pain**
  - Emphasize non-pharmacological treatments
  - Emphasize enhancing function & QOL

- **Evaluate pain etiology carefully**
- **Use non-pharmacological modalities**
- **Assess risk factors for addiction & abuse**
  - Use non-opioids if possible
- **Emphasize improved function & QOL as primary goal of therapy, NOT pain relief**
  - Consider using available tools to assess
  - Involve family, work, etc. to monitor

### Chronic Non-malignant Pain

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- **Use non-pharmacological modalities**
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Chronic Non-malignant Pain

- Use formal pain agreement for informed consent prior to prescribing opioids
  - Include consent for UDS
- Initiate opioids as a therapeutic trial
  - Discontinue (taper or detox) if ineffective or significant aberrant behaviors noted
  - Consider referral for addiction evaluation & treatment
- Monitor function & QOL as primary goal
- Monitor UDS & OARRS reports

Understanding Addiction

- Physical dependence
  - Normal and expected phenomenon
  - Due to decrease in endogenous analogues
  - Characteristic withdrawal syndrome
  - Usually not a serious problem
    - If symptoms improve, drug can be weaned

Aberrant Drug-taking Behaviors

**Steven D. Passik, PhD**

- Probably more predictive
  - Selling prescription drugs
  - Prescription forgery
  - Stealing or borrowing another patient’s drugs
  - Injecting oral formulation
  - Obtaining prescription drugs from non-medical sources
  - Concurrent abuse of related illicit drugs
  - Multiple unsanctioned dose escalations
  - Recurrent prescription losses

- Probably less predictive
  - Aggressive complaining about need for higher doses
  - Drug hoarding during periods of reduced symptoms
  - Requesting specific drugs
  - Acquisition of similar drugs from other medical sources
  - Unsanctioned dose escalation 1-2 times
  - Unapproved use of the drug to treat another symptom
  - Reporting psychic effects not intended by the clinician

Understanding Addiction

- Addiction
  - Psychological/behavioral phenomenon
  - Compulsive use causing physical, psychological, or social harm to the patient
  - Continued use despite such harm
  - Compulsive actions to acquire the drug
  - Rare in terminally ill patients
    - Often note increased level of functioning
### Understanding Addiction

- **“Pseudo-addiction”**
  - Prevalence uncertain & controversial
  - Occurs in patients
    - Whose symptoms are under-treated
    - Who fear medication will be arbitrarily withheld
  - May exhibit aberrant behaviors
    - Hoarding, hostility, manipulation, lying, etc.

### Pain Assessment Mnemonic

- **P** – provoking, palliating factors
- **Q** – quality of pain
- **R** – radiation (from where to where)
- **S** – severity
- **T** – temporal course
  - Long term, including onset & short term

### Pain Assessment

### Intensity of Pain

- Pain is not measurable, hence we must rely on patients subjective descriptions
- Several rating scales of intensity are available, utilizing numbers, colors, faces
  - Mild, moderate, severe, excruciating
- Can suggest objective standard
Summary

- Evaluation of the patient with pain should include:
  - Determination of the clinical characteristics of the pain by careful history and exam
    - Define etiology if possible
  - Determination of the mechanism of the pain
    - Nociceptive, neuropathic, or CRPS
  - Classification as either acute or chronic pain
    - Malignant vs. non-malignant chronic pain

WHO Pain Ladder

1 Mild
- Acetaminophen
- NSAIDs
± Adjuvants

2 Moderate
- Acetaminophen + Codeine
- Acetaminophen + Oxycodone
± NSAIDs
± Adjuvants

3 Severe
- Morphine
- Hydromorphone
- Methadone
- Fentanyl
- Oxycodone
± Acetaminophen
± NSAIDs
± Adjuvants

WHO Ladder Concepts
- By the mouth
- By the clock
- By the ladder
- For the individual
- Attention to detail

Note: Adjuvants may 1) enhance analgesia, 2) treat concurrent symptoms, or 3) provide independent analgesia for specific types of pain

Pharmacologic Treatment of Pain
Sensitivity to Opioids

<table>
<thead>
<tr>
<th>Type of Pain</th>
<th>Opioid Responsiveness</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nociceptive</td>
<td>+ + +</td>
</tr>
<tr>
<td>- Somatic</td>
<td>+ +</td>
</tr>
<tr>
<td>- Visceral</td>
<td>+</td>
</tr>
<tr>
<td>Neuropathic</td>
<td>+</td>
</tr>
</tbody>
</table>

Clearance Considerations

- 90-95% of opioids cleared in urine
- Dehydration, renal failure, severe hepatic failure may cause decreased clearance
- Morphine has an active metabolite (M-6-G) that may accumulate in patients with renal insufficiency
  ✓ Consider an alternate opioid in patients with renal failure, (e.g. oxycodone, hydromorphone, fentanyl)

Opioid Pharmacology

- Conjugated in liver
- Excreted via kidney (90%-95%)
- First-order kinetics
- Cmax after
  ✓ po ≈ 1 h
  ✓ SC, IM  ≈ 30 min
  ✓ IV  ≈ 10-15 min
- Half-life at steady state
  ✓ po / pr / SC / IM / IV  ≈ 3-4 h

Opioid Adverse Effects

Common
- **Constipation**
- Dry mouth
- Nausea / vomiting
- Sedation
- Sweats

Uncommon
- Bad dreams / hallucinations
- Dysphoria / delirium
- Myoclonus / seizures
- Pruritus / urticaria
- Respiratory depression
- Urinary retention
- Opioid-induced neurotoxicity
### Opioid Constipation

- Common to all opioids
  - Effects on CNS, spinal cord, myenteric plexus
  - Easier to prevent than treat
  - Diet usually insufficient
  - Bulk forming agents not recommended

### Opioid-Induced Neurotoxicity (OIN)

- Neuropsychiatric syndrome
- Cognitive dysfunction
- Delirium
- Hallucinations
- Myoclonus/seizures
- Hyperalgesia/allodynia - generalized

### Opioid Constipation

- Stimulant laxative
  - Senna, bisacodyl, glycerine, casanthranol, etc
- Combine with a stool softener
  - Senna + docusate sodium
- Osmotic laxative for refractory cases
  - MOM, lactulose, sorbitol, Miralax

### OIN: Treatment

- Opioid rotation
  - Reduce opioid dose (?)
- Hydration
- Benzodiazepines
- Ketamine, psychostimulants
- Non-opioid therapy
Opioid Naïve Patients

- Start at a low dose & titrate to pain relief
- Opioid doses can be titrated up by 30%-100% or more each day for severe pain
- Until an effective baseline dose can be established, it is best to avoid sustained release or transdermal systems since they cannot be rapidly and accurately titrated.

Equianalgesic Dosing

<table>
<thead>
<tr>
<th>PO/SL</th>
<th>Name</th>
<th>IV/SQ/IM</th>
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</thead>
<tbody>
<tr>
<td>30</td>
<td>Morphine</td>
<td>10</td>
</tr>
<tr>
<td>30</td>
<td>Oxycodone</td>
<td>N/A</td>
</tr>
<tr>
<td>30</td>
<td>Hydrocodone</td>
<td>N/A</td>
</tr>
<tr>
<td>7</td>
<td>Hydromorphone</td>
<td>1.5</td>
</tr>
<tr>
<td>N/A</td>
<td>Fentanyl</td>
<td>0.1</td>
</tr>
<tr>
<td>300</td>
<td>Meperidine*</td>
<td>100</td>
</tr>
</tbody>
</table>

*DO NOT USE

Routine Oral Dosing

Immediate Release Formulations

- For adults >60kg, in moderate to severe pain, start with oral morphine 5 mg equivalent
- May want to start lower for elderly, e.g. 2.5 mg oral equivalent
- Hydrocodone, morphine, hydromorphone, oxycodone oral dosing
  ✓ Dose q 3 to 4 h
  ✓ Adjust dose daily for severe pain

Extended Release Formulations

- Improves compliance, adherence
- Dose q 8, 12, or 24 h (product specific)
  ✓ Don’t crush or chew tablets
- May adjust dose every 2-4 days
  ✓ Once steady state reached
Breakthrough dosing

- Use immediate-release opioids
  - 5%–15% of 24 hour dose
  - Maximum time interval based on half-life
  - Minimum time interval based on $C_{\text{max}}$
    - po / pr $\approx q$ 1 h
    - SC, IM $\approx q$ 30 min
    - IV $\approx q$ 10–15 min
- Do NOT use extended-release opioids

Alternate Routes

- Transmucosal
- Feeding tubes
- Rectal
- Transdermal
- Parenteral
- Intraspinal

Treating Pain – Ideal

Changing Opioids

- Use equianalgesic tables, do not guess!
  - Analogous to changing from IV to oral antibiotics - be precise!
- Incomplete cross-tolerance
  - Start with 50%–75% of published equianalgesic dose
    - More if uncontrolled pain, less if adverse effects
  - Provide adequate breakthrough dosing
Methadone - CAUTION

• SHOULD BE USED WITH CAUTION
• NOT A FIRST LINE OPIOID
• RISKS INCLUDE
  ✓ Progressive increase in drug level over about a week or more, monitor closely for toxicity
  ✓ Exacerbates sleep apnea
  ✓ Prolongation of QT interval, especially at higher doses

Conversion to Methadone

• Daily Oral Morphine Dose Equivalents followed by the Conversion Ratio of Oral Morphine to Oral Methadone
  ✓ <100 mg - 5:1 (5 mg morphine:1 mg methadone)
  ✓ 101-300 mg - 8:1
  ✓ 301-1000 mg - 12:1
  ✓ >1000 mg - 20:1
• Due to incomplete cross-tolerance, it is recommended that the initial dose is 50-75% of the equianalgesic dose.

Methadone for Pain

• Binds to mu and NMDA receptors
  ✓ Decreased opioid tolerance
  ✓ Increased effectiveness for neuropathic pain
• Dose interval for methadone is variable
  ✓ q 6 h or q 8 h usually adequate
  ✓ Duration of analgesia is 6-12 hours
• Extended terminal half-life, up to 190 hours
  ✓ Adjust methadone dose q 4–7 days
  ✓ Use breakthrough medication while titrating dose to avoid severe pain

Common Opioid Errors

• Using extended-release preparations for initial dose titration or breakthrough dosing
• Switching opioids rather than titrating dose
• Failing to distinguish sleepiness caused by exhaustion once pain is relieved or disease process from sedation caused by overmedication (in severe malignant pain)
• Unfounded fear of respiratory depression
Adjuvant Analgesics

• Characteristics of Adjuvant Analgesics
  ✓ Drug with primary indication other than pain
    • Usually “off-label” when used for pain
  ✓ Analgesic in some painful conditions
  ✓ Often used in combination with one or more primary analgesics
  ✓ Evidence for effectiveness variable, but systematic approach dependent on
    • Clinical trials in particular syndromes
    • Systematic clinical experience

Adjuvant Analgesics

• General considerations in the use of AA
  ✓ Assess comprehensively
    • Consider pain, medical condition and psychosocial
    • Consider adverse effects & risks for each patient
    • Requires frequent re-evaluation of the patient
  ✓ Select a drug for a specific indication
    • Depends on characteristics of pain or associated symptom that may respond to the adjuvant

Adjuvant Analgesics

• General considerations in the use of AA
  ✓ Know the pharmacology of the drug selected
    • Know elimination half-life and time-action
    • Know differences for pain vs. primary use
    • Titrate dose over reasonable time frame
  ✓ Recognize inter- & intra- individual variability
    • Sequential trials of different meds in each class
  ✓ Consider the risks of polypharmacy
### Adjuvant Analgesics

<table>
<thead>
<tr>
<th>Type</th>
<th>Examples</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antidepressants</td>
<td>Amitryptyline, nortriptyline, imipramine, desipramine, doxepin</td>
</tr>
<tr>
<td>Antiepileptic drugs</td>
<td>Gabapentin and pregabalin</td>
</tr>
<tr>
<td>Neuroleptics</td>
<td>Antihistamines</td>
</tr>
<tr>
<td>Corticosteroids</td>
<td>Muscle relaxants</td>
</tr>
<tr>
<td>Psychostimulants</td>
<td>Oral local anesthetics</td>
</tr>
<tr>
<td>Adjuvant analgesics</td>
<td>Sympatholytic drugs</td>
</tr>
<tr>
<td>for bone pain</td>
<td>Calcium channel blockers</td>
</tr>
<tr>
<td></td>
<td>Miscellaneous</td>
</tr>
</tbody>
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### Antidepressants

**Indications**
- Most strongly indicated in neuropathic pain or pain associated with depression or insomnia
- Dysesthetic neuropathic pain may respond better than paroxysmal neuropathic pain
- Trials can be justified in virtually every type of chronic pain, if no contra-indications

**Dosing**
- Start low & go slow

**TCAs:**
- Especially amitryptyline, nortriptyline, imipramine, desipramine, doxepin
- Variably effective in headache, arthritis, chronic LBP, PHN, painful DM neuropathy, fibromyalgia, chronic facial pain, psychogenic and idiopathic pain

**SSRIs and novel antidepressants**
- Less compelling evidence, but fewer side effects and easier dosing regimens, especially if patient depressed

### Antiepileptic Drugs (AEDs)

- Gabapentin and pregabalin
  - First line in neuropathic pain
  - Consider trial in all chronic pain syndromes
- Carbamezapine, phenytoin, VPA, clonazepam
  - Especially paroxysmal pains, also dysesthesias
- Newer agents may also be effective
  - Lamotrigine, topiramate, oxcarbazepine, & others
## Website Resources

- [http://www.npecweb.org/default.asp](http://www.npecweb.org/default.asp)
  - The National Pain Education Council
  - Department of Pain Medicine and Palliative Care at Beth Israel Medical Center
- [http://www.eperc.mcw.edu/](http://www.eperc.mcw.edu/)
  - EOL / Palliative Education Resource Center
  - OARRS - Ohio Automated Rx Reporting System