Issues of Pain:
Further questions, and Summary
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A.M.B.E.R. clinic
Albuquerque Multidisciplinary Behavioral Evaluation for Recovery and Resiliency

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Overview

• Pain presentations
• Great mimicry
• Pain-related behavior
• Summary
Multiple Dimensions of Pain

The ABCs of Pain

Affective Dimension

Behavioral Dimension

Cognitive Dimension

Physiological-Sensory Dimension
Definition of Pain

“Unpleasant sensory and emotional experience arising from actual or potential tissue damage or described in terms of such damage (IASP)
Types of Pain

• Nociceptive vs Neuropathic
• Physiologic vs pathophysiologic
• Acute vs chronic
• Malignant vs nonmalignant
• Pain syndromes
Medication Management-- Analgesics

**Analgesics**
Three Types

- **Nonopioids** (acetaminophen, NSAIDS)
- **Opioids** (mu agonist, agonist-antagonist)
- **Adjuvants** (multiple examples) & Anesthetics
Acetaminophen

• Mechanism of action is not certain
• Probably centrally acting—?cox-3 inhibitor
• Acetaminophen toxicity
  • Hepatotoxicity
    • Toxic metabolite (NAPQI)
    • Several other mechanisms lead to hepatotoxicity
    • Mechanism not completely understood
  • Nephrotoxicity >4g/day for long periods
    • Uncertain cause
    • May be caused by activity of NAPQI in renal microsomes
    • Increase frequency to 6-8 hrs in renal failure
NSAIDS

• NSAIDS—Anti-inflammatory, antipyretic, analgesic
• Mechanism of action—prostaglandin inhibition by way of COX-1
  • Prostaglandins
    • important in maintaining integrity of GI and duodenal mucosa; important in modulating renal plasma flow
• Inhibit formation of thromboxane— affecting platelet aggregation
• Use with caution in pts. with history of asthma
  • Inhibits prostaglandin E—responsible for bronchodialation
Transduction: Nociceptive Chemical Stimuli

Arachidonic cascade

Phospholipids released

Trauma

5-Lipoxygenase

Cyclo-oxygenase

Leukotrienes

Prostaglandins

PGI2

PGE2

PGF2

Vasodilation

Antiaggregation

Fever

Pain

Thromboxane A2 platelet aggregation

Vasodilation

Uterine contraction

pain receptor
<table>
<thead>
<tr>
<th>Class</th>
<th>Generic name</th>
<th>UAD</th>
<th>Brand name</th>
</tr>
</thead>
<tbody>
<tr>
<td>Proprionic acids</td>
<td><strong>Naproxen</strong></td>
<td>500 mg initially-followed by 250mg q6-8h</td>
<td>Naprosyn, Anaprox, Alleve Ansaid Ansaid Daypro Motrin Orudis, Orovail Toradol</td>
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<tr>
<td></td>
<td><strong>Flurbiprofen</strong></td>
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<tr>
<td></td>
<td><strong>Oxaprozin</strong></td>
<td>400-800mg Q6-8h</td>
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<tr>
<td></td>
<td><strong>Ibuprofen</strong></td>
<td>25-75 mg Q6-8h</td>
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<td></td>
<td><strong>Ketoprofen</strong></td>
<td>Max 120mg/d (parenteral)</td>
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<tr>
<td></td>
<td><strong>Ketorolac</strong></td>
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<tr>
<td>Indoleacetic acids</td>
<td><strong>Sulindac</strong></td>
<td>200mg Q12h</td>
<td>Clinoril Indocin Lodine</td>
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<tr>
<td></td>
<td><strong>Indomethacin</strong></td>
<td>25-50mg q8h</td>
<td></td>
</tr>
<tr>
<td></td>
<td><strong>Etodolac</strong></td>
<td>200-40mg q6-8h</td>
<td></td>
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<tr>
<td>Class</td>
<td>Generic name</td>
<td>UAD</td>
<td>Brand name</td>
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<td>---------------</td>
</tr>
<tr>
<td>Phenylacetic acids</td>
<td>Diclofenac</td>
<td>50 mg/q8h</td>
<td>Cataflam, Voltaren</td>
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<tr>
<td>Salicylic acids (nanacetylated)</td>
<td>Salsalate</td>
<td>1000-1500 mg/q12h</td>
<td>Disalcid</td>
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<tr>
<td></td>
<td>Choline magnesium trisalicylate</td>
<td>1000-1500 mg/q12h</td>
<td></td>
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<tr>
<td>Naphthylalkanone</td>
<td>Nabumetone</td>
<td>1000-2000 mg/day</td>
<td>Relafen</td>
</tr>
<tr>
<td>oxicam</td>
<td>Piroxicam</td>
<td></td>
<td>Feldene</td>
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</table>
COX-2 Inhibitors

• May have fewer GI effects than COX-1 inhibitors
• Should be avoided in patients with creatinine clearance <30ml/min
  • Carry same risk as traditional NSAIDs
• Celecoxib—Celebrex
  • UAD=100-200 mg q12h max=400 mg/d
Opioids
Mu-agonists

Bind to mu opiate receptors blocking transmission of pain

• Morphine
• Fentanyl
• hydromorphone
• oxycodone
• hydrocodone

• Codeine
• *Methadone
• *meperedine
• *tramadol
Morphine

• Hydrophilic—delayed onset and longer duration
• Two metabolites but only one active at opioid receptor—morphine-6-glucuronide (M6G)—analgesic
  • Patients with renal impairment should start at ¼ dose and titrate as needed
    • Accumulation results in neurologic side effects as well
    • Removed with dialysis
Hydromorphone (Dilaudid)

• Hydrophyllic—similar to morphine
  • IV—1.5 mg:10 mg morphine/PO—7.5 mg:30 mg morphine
    Onset 5 min; peak in 8-20 min. duration ~ 4 hrs
  • Oral
    • 60% bioavailable; onset 30 min. duration 3-4 hrs
    • Metabolized in the liver; Several metabolites

• Use decreased amounts in renal impairment due to possible sensitivity to hydromorphone-3-glucuronide → possible neuroexcitation
  • there is no 6-glucuronide so may have fewer SEs

• May be safer than morphine in renal insufficiency
Fentanyl

• Lipophillic ➞ Short half-life, short duration of action
  • UNLESS given regularly—then half-life is extended
• No active metabolites
• Safer in renal and liver failure
• Fewer side effects
• Half-life extends with continuous use
• Multiple formulations
  • transdermal, oral transmucosal, buccal
Oxycodone

- Available in combination or single-entity
  - Short and Long-acting
- More potent than morphine
- Metabolized in the liver by cytochrome CYP2D6
  - Multiple metabolites
- Binds at $\mu$ and $\kappa$ receptors—may be better in chronic pain states
  - Half-life and bioavailability slightly longer than MS
  - One active metabolite—oxymorphone
  - Women may have a greater effect
  - Excretion impaired in uremic patients and
    - Elimination half-life is severely impaired in these patients
  - May cause CNS toxicity and sedation in renal failure
Hydrocodone (Vicodin)

- Only available in combination with acetaminophen, ibuprofen, aspirin
  - Onset 20 min. peak by 60 min; half-life 3.8 hrs
- Metabolized in the liver
  - Several metabolites
- Significant renal excretion of active forms
- Should be avoided in patients with renal failure
- Adverse effect – hearing loss
Demerol (meperidine)

- Half-life is 2-3 hrs (parenterally)
- Bioavailability from p.o. is ¼ that of parenteral
- Onset 10 minutes; peak effect 30 min. duration up to 4 hrs
- More likely than other opioid drugs to cause delirium in postop pts of all ages
  - More nausea and vomiting
- Limit use to 600 mg/d and no more than 48 hours due to metabolite—normeperedine
- Observe for signs of neuroexcitation—restlessness, shakiness, tremors, twitching and jerking
- Misconception—produces less biliary spasm than other opioids—all opioids can produce this
Normeperidine

• Only active metabolite of meperidine
  • toxic metabolite
  • half-life 15-20 hrs
  • causes neuroexcitation—hyperreflexia, myoclonus, agitation and grand mal seizures
  • half analgesic potency but twice the toxicity
  • Is not reversed with naloxone and may increase risk of seizures if naloxone given

• Use extreme caution in patients with seizure disorder
• Use caution in patients with renal insufficiency
• Contraindicated with MAOI (monoamine oxidase inhibitors)—can cause serotonin syndrome or death
Codeine

• 60mg = 600 mg of aspirin
• Not appropriate for moderate to severe pain
• Usually more constipating
• Has more psychotomimetic effects
• Metabolized in the liver to morphine
  • Several metabolites
  • Metabolism is necessary for analgesia
  • Poor metabolizers may show absence of analgesia
• Reduced renal clearance in advanced renal failure
  • Reports of serious adverse effects in renal failure
Methadone—good news

• Inexpensive
• Adverse effects similar to other opioids
• Rapid onset—30-60 minutes; duration 4-6 hrs; peak effect 2.5 hrs
• ~ 80% bioavailability
• No active metabolites
• Long duration with continued use
• No ceiling dose other than side effects
• Has some SSRI and NMDA antagonist activity
• For opioid naïve patients $\rightarrow$ start at 2.5mg Q8H
• Excreted in feces—considered safe in renal insufficiency
Methadone—not so good news

- Long half-life—15-60 hours-
  - Unpredictable
  - Difficult to titrate
  - Difficult to convert from other opioids to methadone
- Duration initially is 3-6 hrs → 8-12 hr with repeated dosing
- Varied inter-individual effects
- Efficacy is greater with repeated dosing
- Multiple drug-drug interactions that can induce or inhibit effect by other drug or be effected
  - Close observation is required
Dual-mechanism Analgesics

• Tramadol—for mod to moderately severe pain
  • Weak mu-agonist and norepeniphrine and serotonin reuptake inhibitory activity similar to TCAs
  • Peak effect in ~ 2 hrs of 100mg dose
  • Potency equivalent to codeine and five times less potent than morphine
  • Ceiling effect
  • Max dose is 400mg/24h
  • Use with caution in pts w seizures or on SSRIs

• Tapentadol – Nucynta
  • Agonist at mu and blocks reuptake of norepinephrine
  • Schedule II drug
  • Indicated for mod-severe pain
  • Avoid combining with SSRIs
Equianalgesic Dosing Guidelines

• Equianalgesic means approximately the same pain relief
• The chart is a guideline. Titrate meds according to pt’s response
• Chart is helpful when switching from one drug to another or when switching to another route
• Dosages are not necessarily starting doses
• Consider incomplete cross-tolerance
<table>
<thead>
<tr>
<th>Drug</th>
<th>Oral Dose</th>
<th>IV Dose</th>
<th>Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Morphine</td>
<td>30 mg</td>
<td>10 mg</td>
<td>3-5 hours</td>
</tr>
<tr>
<td>Fentanyl</td>
<td>Breakthrough only (OTFC)</td>
<td>100mcg (0.1mg)</td>
<td>0.5-1 hour</td>
</tr>
<tr>
<td></td>
<td></td>
<td>100 mcg/h TD ≈ 4 mg/h IV MS; 1mcg/h TD ≈ 2 mg/24 h oral MS</td>
<td></td>
</tr>
<tr>
<td>Hydromorphine</td>
<td>7.5 mg</td>
<td>1.5 mg</td>
<td>2-4 hours</td>
</tr>
<tr>
<td>Meperidine</td>
<td>300 mg NR</td>
<td>75-100 mg</td>
<td>2-4 hours</td>
</tr>
<tr>
<td>Codeine</td>
<td>200 mg NR</td>
<td>130 mg</td>
<td>3-4 hours</td>
</tr>
<tr>
<td>Methadone</td>
<td>---</td>
<td>---</td>
<td>---</td>
</tr>
<tr>
<td>Oxycodone</td>
<td>20-30 mg</td>
<td>---</td>
<td>3-4 hours</td>
</tr>
<tr>
<td>Hydrocodone</td>
<td>30 mg</td>
<td>---</td>
<td>3-4 hours</td>
</tr>
<tr>
<td>Nalbuphine</td>
<td>---</td>
<td>10 mg</td>
<td>3-6 hours</td>
</tr>
</tbody>
</table>
First-line Drugs in Chronic Pain

- **Gabapentin (Neurontin)**—start w/ 100-300 mg/day Usual Effective Dose (UED) 300-3600 q8h
- **Pregabalin (Lyrica)**—start with 100-150 mg/day; UED 150-600 q12h
- **SNRI**
  - **Duloxetine (Cymbalta)**—start w/ 30 mg/day; UED 60 mg q12h
ADJUVANT ANALGESICS:
MAJOR CLASSES

• Anticonvulsants
• Antidepressants
• Psycho-stimulants
• Muscle relaxants
• Sedatives
Opioid Side Effects

• Nausea and vomiting
• Pruritus
• Urinary retention
• Mental status changes
• Sedation
• Respiratory depression
Opioid Induced Constipation

• The hand that writes the prescription for an opioid and
• Fails to write the order for a laxative should be
• The hand that removes the impaction
Balanced Analgesia

- Inter-disciplinary approach
  - Medication management
  - Physical activity
  - Maximize nutritional contributions
  - Mental health
  - Support group
  - Spirituality
Non-Pharmacologic Interventions

• Increase activity

• Individualize interventions
  • music
  • artwork
  • humor

• Address constipating effects of opioids
Non-Pharmacologic Interventions

• Increase activity
• Individualize interventions
  • music
  • artwork
  • humor
• Address constipating effects of opioids
To summarize:

• Treat pain initially aggressively—
  • ***Titrate to Effect

• Adequate analgesia results in:
  • Early participation in activity
  • Prevention of complications
  • Decrease risk of chronic pain
  • Early return to individual level of functioning

• Use assessment tool specific to population

• Always combine modalities— opioids with nonopioids and pharmacologic with non-pharmacologic
Team

• Purpose
  • Keeping individual separated?
  • Safety?
  • Support? Change in functioning?

• Respect - has to be evidenced, consistent
  • Individuals
  • Health goals
  • Institutional goals
  • Societal expectations
Team

• Communication
  • Verbal/written
  • One point
  • Frequency; emergency

• Responsibilities
  • Defined roles by training
  • Acquired roles by ability or habit
  • Guardianship/consent
Course summary

• Holistic view of patients
• Integrate context and communication
• Be creative in approaches
• Document strategies
• Keep raw data and observations clear from interpretations
Many thanks for your participation, comments, feedback and ongoing hard work!

This was the last in this series.

Resources and back issues can be found at Continuum of Care website:
http://som.unm.edu/coc/Training/powerpointnew.html