Surgery on the Chronic Pain Patient

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Disclosure Statement

- I do not have relevant financial relationships with commercial interests related to the content of this presentation.
Learning Objectives

• Review of the biochemistry of pain
• Review pharmacological options
• Discuss chronic pain conditions requiring poly-pharmacy
• Identify high risk patients for postoperative pain and respiratory depression
• List the important perioperative goals for the chronic pain patient
• Definition
  – “Unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage.” – IASP

• Somatosensation v. Nociception v. Pain
Presentations of Pain

- Acute/Chronic
- Central pain
- Complex regional pain syndrome I and II
- Deafferentation pain
- Dysesthesia
- Fibromyalgia
- Hyperalgesia
- Neuralgia/Neuritis
- Neuropathic
- Radicular/Radiculopathy
Presentations of Pain

- Neuropathic pain
  - Diabetic neuropathy
  - Postherpetic neuralgia
  - Central neuropathic pain
  - Spinal cord injury
  - Complex regional pain syndrome
  - HIV associated peripheral neuropathy
- Burning, lancinating, tingling
- Hyperexcitability in central and peripheral neurons
Pain Neurochemistry

- **Transduction**
  - Energy converted to electrical impulses
- **Transmission**
  - Dorsal Root Ganglion
  - Spinal Neurons (Abeta, Adelta, C)
  - Brainstem
- **Modulation**
  - Gate control theory
  - Central Sensitization
- **Perception**
  - Primary and Secondary somatosensory cortices, insula, anterior cingulate cortex, prefrontal cortex, thalamus
Pain Neurochemistry

• Peripheral inflammatory factors
  – Bradykinin
  – Acidic environment
  – Serotonin
  – Histamine
  – Eicosanoids
  – NO
  – Adenosine
  – Cytokines
  – Chemokines
  – Excitatory amino acids
  – Nerve growth factor
Pain Neurochemistry

• Peripheral antihyperalgesics
  – Opioid receptors
  – ACh
  – GABA
  – Somatostatin
Pain Neurochemistry

• Pain transmission
  – Excitatory neurotransmitters
    • Glutamate
    • Aspartate
    • Subtypes
      – N-methyl-D-aspartate
      – Non NMDA
    • P2X receptors (ATP)
  – Inhibitory neurotransmitters
    • Glycine
    • GABA (a, b, c*)
    • Serotonin (descending)
    • Norepinephrine (descending)
    • Adenosine
    • ACh
  – Neuropeptides
Pharmacology

- Opioids
- NSAIDs
- Antidepressants
- Membrane stabilizers
Opioids

• Short acting
  – Codeine, hydrocodone, morphine, oxycodone, oxymorphone, hydromorphone

• Sustained Release versions

• Long-acting
  – Methadone
Opioids

- Mild to moderate pain
  - Tramadol
    • Mu agonism, Serotonin and NE reuptake inhibitor
    • Supoptimal pain control usually requiring adjuvant medications
  - Tapentadol
    • Maximum recommended dose 600mg daily
    • 100mg ~ 15mg oxycodone IR
  - Codeine
    • metabolism to active analgesic compounds
  - Hydrocodone
  - Oxycodone
    • 1.5-2x more potent than morphine
Opioids

- Morphine
  - ~3:1 oral to IV (ie 10mg oral ~ 3.3 mg IV)
  - 10:1 oral to epidural
  - 100:1 oral to intrathecal
Opioids

• Fentanyl
• Transdermal
  – 25mcg/h: 135mg oral morphine equivalent (20mg q4h)
  – 50mcg/h: 135-224mg (25-30mg q4h)
  – 75mcg/h: 225-314mg (40-50mg q4h)
  – 100mcg/h: 314-404mg (55-60mg q4h)
Opioids

• Methadone
  – Advantages: low cost, no metabolites
  – Disadvantages: stigma, difficult to initiate/maintain/convert, cardiac arrhythmias
  – Mechanism of Action
    • NMDA antagonist
    • Serotonin and NE reuptake inhibitor
    • Mu-opioid agonist
  – Opioid naive: 2.5mg q8h, weekly dose changes
Buprenorphine

- Binds tightly to mu-receptors
- Partial agonist
- Competitive antagonism to other opioids
- Opioid addiction therapy
- 24-60h at the receptor
- Limited effectiveness of other agents
- Hold if possible prior to surgery
- Restart after patient is opioid-free 24h to avoid withdrawal (approved buprenorphine provider)
Opioids

• Considerations
  – Endocrine abnormalities
  – Sleep disordered breathing
  – Opioid induced hyperalgesia
Antidepressants

• Tricyclic Antidepressants
  – Serotonin and NE reuptake inhibition
  – Useful in diabetic neuropathy, CRPS, chronic headache, poststroke pain, radicular pain
  – Analgesia independent of antidepressant effects
  – Side effects secondary to antihistaminergic and anticholinergic effects
  – Considerations
    • Decrease the seizure threshold
    • Potentially proarrhythmic (>40 y/o check QTc interval, 450ms)
    • SSRIs increase TCA plasma levels
  – Mitigated by starting at low doses
Antidepressants

- **Starting doses**
  - Amitriptyline 10-25mg qday
  - Nortriptyline 10-25mg qday
  - Desipramine 10-25mg qday
  - Doxepin 10-25mg qday
Antidepressants

• Serotonin-Norepinephrine Reuptake Inhibitors
  – Less anticholinergic or antihistaminergic effects
  – Modest efficacy in neuropathic pain states
  – Laboratory studies not necessary
Antidepressants

• Duloxetine
  – 30mg qday starting dose
  – Approved for diabetic PN, fibromyalgia, major depression, generalized anxiety disorder
  – Not to be used in renal or hepatic impairment

• Venlafaxine
  – 37.5mg qday starting dose
  – Watch in patients with hypertension at doses over 150mg qday
Membrane Stabilizers

• Anticonvulsants
  – Phenytoin: diabetic neuropathy (not first line)
  – Carbamazepine: trigeminal neuralgia, post-stroke pain, postherpetic neuralgia, diabetic neuropathy
    • 100-200mg bid, maintenance usually 600-800mg daily
    • Pancytopenia, Stevens-Johnson syndrome, Toxic epidermal necrolysis
  – Oxcarbazepine (Trileptal): better side effect profile
Membrane Stabilizers

• Calcium Channel Blockers
  – Decreased release of glutamate, NE, substance P
  – Gabapentin: PHN, CRPS, DN, lumbar stenosis, MS; not as effective in phantom limb pain
    • 100-300mg daily, 3600mg/day max
      – Fatigue, somnolence, dizziness
      – 2 months may be needed
  – Pregabalin; 150mg/day 2-3 dosing interval, max 600mg/day
    • PHN, DN
Non-opioid Analgesics

- NSAIDs
- COX-2 inhibitors
- Acetaminophen
Non-opioid Analgesics

- **Aspirin**
  - 600-1500mg QID
  - Inactivates COX permanently

- **NSAIDs**
  - Propionic Acid
    - Naproxen: peak 4-6h, 250-500mg BID
    - Ibuprofen: peak 1-2h, 200-800mg QID (Caldolor 800mg IV q6h)
    - Ketoprofen: 1-2hr 50-75mg TID
Non-opioid Analgesics

• NSAIDs
  – Acetic Acid
    • Diclofenac (COX2 selective), 50mg - 75mg BID-QID
    • Etodolac (some degree – less GI upset), 200-300mg BID-QID, 15-20mg/kg/day
    • Ketorolac: oral peak 1-2h, 30mg IM ~ 12 mg morphine, 100mg meperidine,
      – Do not use in hypovolemic elderly pts, underlying renal disease, >3-5 days
      – IV 30-60mg then 15-30mg daily dose, oral <=60mg
      – Oral 10mg q6h QID
    • Nabumetone: prodrug, single dosing, arthritis; 500-750 BID
Non-opioid Analgesics

• Anthrilic Acid
  – Meloxicam (COX2 selectivity)
    • 7.5mg daily, 15mg less selective
    • 5-10h peak

• COX2 inhibitors
  – Celecoxib only one available
    • Also have central analgesic effect (lipophilic)
    • 2-3hr peak,
    • Does not interfere with PLT aggregation
    • Osteoarthritis, RA, postoperative pain
  – Etoricoxib (not available) very high selectivity
NSAIDs
NSAIDs

• Overall concerns
  – Renal impairment with NSAIDs
  – Hepatotoxicity
    • Risk factors: concomitant depression, chronic pain, alcohol/narcotic use
  – Cardiovascular → imbalance of TX and Prostacyclin → thromobogenic environment
Non-opioid Analgesics

- Acetaminophen
  - Inhibits central PG synthesis
  - Weak anti-inflammatory effects
  - Poor ability to inhibit COX
  - 1st line for elderly pts
Preoperative Goals

- Multidisciplinary approach
- Establish daily intake (oral, transdermal, sublingual)
- Buprenorphine and methadone considerations
- Oral medications should be continued preoperatively
- Patches: remove prior to surgery
- Intrathecal pumps: no changes
- Consider preemptive analgesia
Preemptive Analgesia

• Theory: block the development of pain before it is produced
• Pain may lead to changes related to neuroplasticity
• Primary phase: stimuli related to surgical injury
• Secondary phase: ongoing stimuli from chemical milieu
• Studies have supported theory but not consistent results
Intraoperative Goals

• Larger doses of opioids may be needed in the chronic pain patient due to tolerance

• Implement opioid-sparing techniques
  – NSAIDs
  – Regional techniques

• Consider non-opioid infusions

• Local Anesthetic Wound infusions
Nonopioid Infusions

• Ketamine
  • Pros: analgesia, maintenance of respiration
  • Cons: postop malaise, accumulation of metabolites
    – Bolus 0.5-1mg/kg at induction, 40-100mcg/kg/min
      • Loftus et al: reduction in morphine consumption at 48h
    – Bolus with infusion more efficacious than bolus alone
    – Most studies demonstrated no increase in side effects
    – Adjuvant for epidural analgesia .05-.25mg/kg/hr
    – Ineffective with TIVA
Non-opioid infusions

• Lidocaine
  – Peripheral and central effects
  – Studies mainly involved abdominal surgery
  – Bolus 100mg-1.5mg/kg with 2-3mg/min infusion prior to surgery and continued 24h postop
  – Ability to suppress the inflammatory processes
  – Lower pain scores, less opioid consumption, reduced hospital stay, faster return of bowel function
  – Did not apply to total hip surgeries and CABG (one study)
Postoperative Goals

• Use equianalgesic doses for those using patches
• Minimize risk of withdrawal by maintaining preoperative baseline requirements
  – More or less may be required depending on type of surgery
• Monitoring: inadequate relief (frequent pain assessments), withdrawal symptoms, excessive sedation, respiratory depression
• Do not attempt to withdraw opioids in the perioperative period
• Postoperative skeletal muscle relaxants
Pain Assessment

• Self-reporting Scales
  – Verbal rating scales
  – Numeric rating scales
  – Visual Analog Scales
  – Questionnaires
  • McGill Pain Questionnaire (MPQ)

• Bias in measuring pain
Myofascial Pain

- TCAs, Gabapentin/Pregabalin
- Skeletal Muscle Relaxants
  - Cyclobenzaprine 5-10mg (usually TID)
  - Chlorzoxazone 250mg TID
  - Carisoprodol 250-350mg QID
  - Methocarbamol 750mg q6H
  - Tizanidine 2mg q8h
  - Baclofen 5mg TID
- Adverse side effects
  - Dry mouth, drowsiness, headache, somnolence
Myofascial Pain

• Benzodiazepines
  – Evidence is moderate
  – Adverse effect profile
  – Not routinely used
  • Diazepam
  • Clonazepam
  • Alprazolam
  • Lorazepam
Chronic Pain After Surgery

Figure 3. Schematic illustration of the processes involved in the development of chronic postsurgical pain and pain disability showing relationships (arrows) among preoperative, intraoperative and postoperative factors. Lines with double arrows between variables show associative relationships reported in the literature. Lines with a single arrowhead show causal relationships based on randomized controlled trials of preventive analgesia.
Inpatient Management

- Initiation or continuation of opioid PCA
- Discontinue oral medications if pain is not controlled and adjust PCA accordingly
- Continuation or initiation of opioid-sparing techniques
  - NSAIDs
  - Regional blocks
- Low dose ketamine infusions
  - Not for pts with hepatic impairment
  - 10-25mg/hr (~0.25-0.5mg/kg LBW)
- Initiation of adjuvant modalities
  - Amitriptyline
  - Gabapentin
  - Pregabalin
  - Transdermal NSAIDs or Lidocaine
Patient Controlled Analgesia

• Pros:
  – Patient can easily administer and titrate
  – Sedation usually occurs prior to respiratory depression

• Cons:
  – Poor understanding leading to suboptimal control
  – Susceptible to operator error

• IV, epidural, peripheral blocks

• IV: continuous basal rate usually reserved for cancer patients
IV PCA

- Fentanyl: 0.015-.05mg bolus, q3-10min
- Hydromorphone: 0.1-0.5mg, q5-15 min
- Morphine: 0.5-3mg, q5-20 min
- Oxymorphone 0.2-0.8mg, q5-15min

* Initial bolus to control pain is necessary.
Referral to Outpatient Clinic

- Chronic pain after surgery
- Evaluate for diagnostic blocks
  - Lumbar pain
  - SI joint injections
  - Facet joint blocks
  - Selective sympathetic blockade
- Evaluate and treat other chronic pain states
Sample Cases

• Patient with fibromyalgia and depression presents for a laparoscopic cholecystectomy in the outpatient setting.
  – Does she take her medicines that morning?
  – When will she restart her meds safely?
Sample Cases

- 42 year old woman with intestinal obstruction presents for an exploratory laparotomy. She is a well-known patient with chronic pain syndrome, multiple back surgeries and fusion at multiple levels. Her medications consists of:
  - Fentanyl patch
  - Morphine PO prn
  - Lidoderm patches
Sample Cases

• 50 year old woman with bilateral wrist tenosynovitis and multiple joint pains had surgery on one of her wrists. She was on multimodal pain therapy before surgery. Along with a nerve block for the operated wrist, the patient was placed on a Dilaudid PCA.

  – On POD 2, she was found sleepy with respiratory rate of 6-8 breaths/min. PCA discontinued and patient improved.
Questions
# Opioid Conversion Table

<table>
<thead>
<tr>
<th>Drug</th>
<th>Route</th>
<th>Equianalgesic Dose (mg)</th>
<th>Duration (h)</th>
<th>Plasma Half-Life (h)</th>
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</thead>
<tbody>
<tr>
<td>Morphine</td>
<td>IM</td>
<td>10</td>
<td>4</td>
<td>2-3.5</td>
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<tr>
<td>Morphine</td>
<td>PO</td>
<td>30</td>
<td>4</td>
<td>4</td>
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<tr>
<td>Codeine</td>
<td>IM</td>
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<td>3</td>
</tr>
<tr>
<td>Codeine</td>
<td>PO</td>
<td>300</td>
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<tr>
<td>Oxycodone</td>
<td>IM</td>
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</tr>
<tr>
<td>Oxycodone</td>
<td>PO</td>
<td>30</td>
<td>3-4</td>
<td>4</td>
</tr>
<tr>
<td>Hydromorphone (Dilaudid)</td>
<td>IM</td>
<td>1.5</td>
<td>4</td>
<td>2-3</td>
</tr>
<tr>
<td>Hydromorphone (Dilaudid)</td>
<td>PO</td>
<td>7.5</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>Meperidine</td>
<td>IM</td>
<td>75</td>
<td>3-4</td>
<td>2</td>
</tr>
<tr>
<td>Meperidine</td>
<td>PO</td>
<td>300</td>
<td>3-4</td>
<td>normeperidine</td>
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<tr>
<td>Methadone</td>
<td>IM</td>
<td>10*</td>
<td>6-8†</td>
<td>12-24</td>
</tr>
<tr>
<td>Methadone</td>
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<td>20*</td>
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<tr>
<td>Hydrocodone</td>
<td>PO</td>
<td>30</td>
<td>3-4</td>
<td>4</td>
</tr>
</tbody>
</table>


*The equianalgesic dose of methadone compared to other opioids is extremely variable with chronic dosing. Conversion from oral morphine to oral methadone may range from 4 to 14:1.
† Risk of CNS depression with repeated use; accumulation in elderly or persons with impaired renal function with regular dosing. Monitor for patient variability in duration of efficacy.


