What a Pain!
A Review of Post-operative Pain Management
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Pharmacy Grand Rounds
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Objectives

• Review multi-modal approach for pain control in a surgical patient

• Outline treatment recommendations for complex post-operative pain management patients

• Assess surgery as a risk factor for prolonged chronic opioid use beyond the post-operative period
Post-operative Pain

• More than 80% of surgical patients experience acute postoperative pain

• Inadequate pain control affects:
  • Quality of life
  • Functional recovery
  • Risk of post-operative complications
  • Risk of persistent postsurgical pain

Pain Management: Multi-modal Approach
Pain Management: Multi-modal Approach

- Simultaneous use of ≥ 2 analgesics which act at different sites in the central and peripheral nervous system

- **Goal:**
  - Reduce pain
  - Minimize opioid use and side effects

Multi-modal: Pre-operative

- Use of pre-operative medications
  - Non-opioid analgesics
    - Celecoxib
    - Acetaminophen
  - Co-analgesics
    - Gabapentin, pregabalin
- Confirm adherence and last dose of home medications
  - Opioids
  - Benzodiazepines
## Common Medications Used

<table>
<thead>
<tr>
<th>Location of Action</th>
<th>Mediators</th>
<th>Inhibitors</th>
</tr>
</thead>
<tbody>
<tr>
<td>Local tissues</td>
<td>Prostaglandins; bradykinin; substance P</td>
<td>NSAID/COX-2 inhibitors; local anesthetics</td>
</tr>
<tr>
<td>Peripheral tissues</td>
<td>Unmyelinated C fibers; myelinated A fibers</td>
<td>Local anesthetics</td>
</tr>
<tr>
<td>Spinal cord</td>
<td>Dorsal root ganglion; dorsal horn</td>
<td>Opioids, gabapentinoids, α-agonists, NMDA antagonists</td>
</tr>
<tr>
<td>Brain</td>
<td>Spinothalamic tracts; cortex</td>
<td>Opioids, acetaminophen, NSAIDs, α-agonists, NMDA antagonists</td>
</tr>
</tbody>
</table>

Figure-Kehlet H. Anesth Analg 1993;77:1049.
Multi-modal: In the OR

- **Neuraxial Therapies**
  - Epidural analgesia with local anesthetics (+/- opioids)
  - Spinal analgesia (intrathecal opioid)

Multi-modal: Post-operative use in ERAS

- **ERAS** (enhanced recovery after surgery)
  - Process used to achieve early recovery after a surgical procedure

http://www.aana.com/resources2/professionalpractice/Pages/Enhanced-Recovery-After-Surgery.aspx

Guidelines on the Management of Postoperative Pain

Management of Postoperative Pain: A Clinical Practice Guideline
From the American Pain Society, the American Society of Regional Anesthesia and Pain Medicine, and the American Society of Anesthesiologists’ Committee on Regional Anesthesia, Executive Committee, and Administrative Council

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Updated Guideline Clinical Pearls

• Oral administration of opioids is generally preferred for pain management of postoperative pain (Recommendation 10)

• Initiation of long-acting oral opioids are generally not recommended or labeled for immediate postoperative pain use (Recommendation 10)

• Use IV patient-controlled analgesia (PCA) if IV route is needed (Recommendation 12); though without a basal rate in opioid-naïve patients (Recommendation 13)

• Use of acetaminophen and/or NSAIDs should be used as part of multimodal analgesia to manage postoperative pain in patient without contraindications (Recommendation 15)

Chou R et al. JPain 2016;17:131-157
Self-Assessment Question #1

Multi-modal approach to pain control:

A. Only should be utilized once a patient is on a post-operative floor

B. Uses ≥ 2 analgesics with different mechanisms of action to optimize pain control

C. NSAIDs should always be used to allow for optimization of pain control

D. B & C
Post-operative Pain Management: Patients with Prior Opioid Use and Abuse
Opioid Use in the U.S.

• 1 out of 5 patients with non-cancer pain or pain-related diagnoses are prescribed opioids

• From 2007 – 2012, the rate of opioid prescribing has steadily increased
  • Surgery (37%)

• 20.5 million Americans with a substance use disorder (2015)
  • 2 million involving prescription pain relievers

Daubress et al. Medical Care 2013; 51(10): 870-878
2015 National Survey on Drug Use and Health.
HHS Publication No. SMA 16-4984, NSDUH Series H-51
Prior Opioid Use + Having Surgery

• With increasing opioid use in the US, more patients have had prior exposure to opioids
  • History of chronic pain
  • Current or history of substance abuse

• Acute surgical pain + baseline pain/opioid exposure

• **Patient specific factors**
  • Is their pain controlled prior to surgery?
  • Is surgery supposed to eventually improved pain control?
  • Confirm dose/strength and current total daily use (long acting and break-through opioids)
Patient Case #1

- 42 yo female here for laparoscopic total colectomy with end ileostomy
- PMH: depression, chronic lower back pain, steroid-refractory ulcerative pancolitis

Home medication list:
- Duloxetine EC 60mg 1 tablet qday
- Oxycodone CR 20mg BID
- Oxycodone 10-15mg q4hrs prn
- Adalimumab 40mg every other week
- Prednisone 40mg daily

- Medication allergies: NSAIDs- GI upset
Peri-operative Pain Management Plan

- Pre-op: multimodal-acetaminophen, celecoxib, gabapentin
- In OR: intrathecal hydromorphone given (spinal)
- Initial post-operative orders (CRS ERP)
  - Oxycodone 5-10mg q6hrs prn pain
  - Acetaminophen 1000mg q6hrs
  - Ketorolac 15mg q6hrs x 4 doses followed by Ibuprofen 600mg q6hrs after
Patient Case #1: POD 0

• Initial interventions to current orders?
  • Restart home meds
    • Duloxetine EC 60mg 1 tablet daily
    • Oxycodone CR 20mg BID (per pain service)
    • Oxycodone 10-15mg q4hrs prn (per pain service, +/- POD 0)
  • Ensure break-through options
    • PCA (per pain service)
Patient Case #1: POD 3

- Transitioning off of the PCA
  - Review past 24hr use of PCA
    - Hydromorphone PCA
      - 0.4mg IV every 10 minutes, 8mg lockout every 4 hours
      - Pain scores 4-7, comfort goal 4

<table>
<thead>
<tr>
<th>Medication</th>
<th>POD 1</th>
<th>POD 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hydromorphone PCA</td>
<td>24 mg</td>
<td>18 mg</td>
</tr>
</tbody>
</table>

What is your oral pain regimen recommendation?
Patient Case #1: POD 3

- Transitioning off of the PCA
- Review past 24hr use of PCA
- Hydromorphone PCA
  - 0.4mg IV every 10 minutes, 8mg lockout every 4 hours
- Pain scores 4-7, comfort goal 4

What is your oral pain regimen recommendation?

### Equianalgesic Opioid Dosing

<table>
<thead>
<tr>
<th>Drug</th>
<th>Equianalgesic Doses (mg)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Parenteral</td>
</tr>
<tr>
<td>Morphine</td>
<td>10</td>
</tr>
<tr>
<td>Buprenorphine</td>
<td>0.3</td>
</tr>
<tr>
<td>Codeine</td>
<td>100</td>
</tr>
<tr>
<td>Fentanyl</td>
<td>0.1</td>
</tr>
<tr>
<td>Hydrocodone</td>
<td>NA</td>
</tr>
<tr>
<td>Hydromorphone</td>
<td>1.5</td>
</tr>
<tr>
<td>Meperidine</td>
<td>100</td>
</tr>
<tr>
<td>Oxycodone</td>
<td>10*</td>
</tr>
<tr>
<td>Oxymorphone</td>
<td>1</td>
</tr>
<tr>
<td>Tramadol</td>
<td>100*</td>
</tr>
</tbody>
</table>

*Not available in the US

McPherson ML. Demystifying Opioid Conversion Calculations: A Guide For Effective Dosing. Amer Soc of Health-Systems Pharm, Bethesda, MD, 2010. Copyright ASHP, 2010. Used with permission. NOTE: Learner is STRONGLY encouraged to access original work to review all caveats and explanations pertaining to this chart.
Patient Case #1

• Recommendation:
  • Oxycodone CR 20mg BID (continued)
  • Oxycodone 10-20mg q3hr PRN
  • Hydromorphone IV 0.4mg q4hrs PRN
  • Acetaminophen 1000mg q6hrs
  • Ibuprofen 600mg q6hrs

• Why not use prn hydromorphone?
• Tip: Reassess — reassess — reassess!
General Pain Management Considerations

• Is pain still an issue?
  • Additional inpatient considerations
    • Location of pain
      • Incisional, neuropathic
    • Frequency vs. dosage
    • Absorption issues?
  • Pharmacogenetic considerations
  • Pain consult service involvement
Patient Case #2

- 55 yo male here for a total R knee arthroplasty
- PMH: chronic lower back & knee pain, hypertension

Home medication list:
- Methadone 10mg q8hrs
- Hydromorphone 8mg q4hrs prn
- Amlodipine 10mg qday
- Senna-S 8.6/50 2 tabs qhs prn
Methadone

• **MOA:** synthetic opioid analgesic with agonist activity at the mu receptor, antagonist at NMDA receptor

• **Pharmacokinetic considerations**
  - **Onset of action:** 30-60 min., peak effect at 2-3 hrs
  - **Analgesic duration:** 8hrs, full analgesic effect seen in 3-5 days
  - **Metabolism:** primarily hepatic (CYP3A4), no active metabolites, excreted 50% fecally, 50% renally
Methadone Clinical Pearls

• Avoid increasing methadone to treat acute surgical pain

• Avoid failing to continue chronic methadone dosing (patient should take morning of surgery)
  • 1 (IV): 2 (PO) ratio
  • Withdrawal possible in 1-3 days

• Frequency of dosing usually indicates indication
  • Chronic pain vs. substance abuse treatment

• Not appropriate for PRN dosing

• ADRs: QTc prolongation, hypotension, serotonin syndrome
Patient Case #2

• During this patient’s medication history pre-surgical admission interview, he discloses his last dose of methadone was the day prior with dinner.
  • Current pain score: 6/10 (baseline 5/10)
  • Patient now is concerned about not taking his AM dose of methadone
  • Patient is a “first case” for the OR today
Self-Assessment Question #2a

• What would be the preferred way to address the patient’s concern pre-operatively?

A. Obtain order from surgery service for a dose equivalent recommendation of oxycodone x1 dose in AM admit

B. Confirm with patient it was ok not to take her morning methadone dose

C. Page the anesthesiologist for patient’s OR room re: patient’s concern

D. None of the above
Patient Case #3

- 58 yo female here for bilateral mastectomy for treatment of breast cancer
- PMH: depression, h/o substance abuse, hypothyroidism

Home medication list:
- Buprenorphine/naloxone 16mg-4mg SL daily
- Sertraline 100mg daily
- Levothyroxine 88mcg daily

Allergy: morphine- ‘itching’
Buprenorphine/Naloxone

• MOA:
  • Buprenorphine: mu-opioid receptor partial agonist and a kappa opioid receptor antagonist
  • Naloxone: mu-opioid receptor antagonist*
    • 4:1 ratio of buprenorphine/naloxone

• Dosing range: 2mg/0.5mg-32/8mg

• Pharmacokinetic considerations
  • Onset of action (SL): 1-1.5hrs
  • Metabolism: hepatic mainly via CYP3A4-mediated N-dealkylation, glucuronidation
  • Elimination half-life (SL): 24-42hrs (buprenorphine), 2-12hrs (naloxone)
  • ADRs: headache (long-term use 30%), nausea, constipation, abdominal pain
Patient Case #3

• During this patient’s medication history pre-surgical admission interview, patient discloses her last dose of buprenorphine/naloxone was this morning with her other medications.

  • She didn’t think she was given a plan about holding any of her medications pre-operatively.
Buprenorphine/Naloxone: Post-op options

• Was it discontinued pre-op?
  • Ideal time frame: held 3 days prior to surgery
    • Option 1: Taper down over 2-3 weeks
    • Option 2: Rapid taper off
      • Has higher withdrawal potential
      • Also bridge with alternative opioids if needed

• Discharge/Outpatient
  • Use of an induction protocol to re-initiate after acute surgical pain resolves
Buprenorphine/Naloxone: Post-op options

• Was it NOT discontinued pre-op?
  • Continue maintenance dose of Buprenorphine/Naloxone

• Treat acute surgical pain with additional opioids
  • Consider opioids with higher intrinsic mu activity
  • Higher likelihood to require a PCA post-op
  • Close monitoring for sedation and respiratory depression

Mayo Policy Reminder

• Methadone, Buprenorphine and other Narcotic Drug Use for Detoxification or Maintenance Treatment of Opioid Dependence Policy, PC.66
  • Treatment of Narcotic Addiction or Withdrawal as a Secondary Condition of Patient Hospitalized for Treatment of Other Problems (Adjunct Treatment)
    • “Treatment by physician without addition treatment waiver is possible”
    • “Maintenance or detoxification treatment must stop once the patient’s primary condition resolves.”
  • Treatment of pain
    • “may be used to treat pain when other treatment modalities have been ineffective or are believed to be inadequate given the nature of the condition”
Self-Assessment Question #2b

• What would be the preferred initial management of post-operative pain in our patient that took their buprenorphine/naloxone 16mg/4mg pre-operatively?

A. Continue buprenorphine/naloxone; Add: multi-modal techniques, fentanyl IV push prn, buprenorphine prn,

B. Continue buprenorphine/naloxone; Add: multi-modal techniques, fentanyl PCA, tramadol

C. Continue buprenorphine/naloxone; Add: morphine PCA, oxycodone prn, tramadol

D. Discontinue buprenorphine/naloxone; Add: multi-modal techniques, hydromorphone PCA, oxycodone prn
Buprenorphine/Naloxone: After POD1

• Reassess—Reassess—Reassess
• Is a pain consult needed?

Therapy adjustment options (beyond opioid dose $\uparrow$)
• Divide buprenorphine/naloxone total daily dose to 3-4x/day dosing
• Consider additional adjunctive options
  • gabapentin/pregabalin, benzodiazepines low-dose ketamine infusions, tricyclic antidepressants, muscle relaxants, gabapentin/pregabalin, benzodiazepines, liposomal bupivacaine injections

• New direction
  • Discontinue buprenorphine/naloxone
Is Surgery a Risk Factor for Prolonged Opioid Use?
Surgery Patients at Risk for Opioid Use
— Among opioid-naive patients, surgery may predispose to chronic use

Surgeries found to increase risk of chronic opioid use

A new study reinforces the need for surgeons and physicians to monitor patients' use of painkillers following surgery and use alternative methods of pain control whenever possible.

A study of health insurance claims showed that patients undergoing 11 of the most common types of surgery were at an increased risk of becoming chronic users of opioid painkillers, according to researchers at the Stanford University School of Medicine.

Study: Risk For Opioid Abuse Increases Following Surgery

Published On: July 11, 2016 7:03 PM

Filed Under: Dr. Max Gomez, heroin, Opioids, Prescription Pain Killers

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Clarke et al. BMJ 2014
- Population based cohort study
- Opioid use after 90 days
- 11 types of major elective surgery
- Exclusion criteria: prior pain/palliative care treatment in last year

Soneji et al. JAMA 2016
- Follow-up study to measure rates of ongoing opioid use up to 1 year after major surgery.

Sun et al. JAMA 2016
- Population based cohort study-surgery and non-surgery comparator group
- Opioid use after 90 days – 365 days
- 9 types of minor and major surgery
- Identification of additional concurrent risk factors for chronic opioid use
- Exclusion criteria: >1 surgery in time frame reviewed

Is Surgery a Risk Factor for Prolonged Opioid Use?

• **Results:**
  • Beyond 90-days post-operative period: 3-6%
  • Beyond 365 days post-operative period: <1%

• **Patient discussion points:**
  • A risk factor yes; but rare
  • Appropriate acute pain control should be the focus not risk of prolonged opioid use
  • Awareness is beneficial
    • Particularly for patients with multiple other risk factors

Discharge Considerations

- Setting appropriate expectations and goals for pain management
  - Address at pre/post-operative appointment
  - Identification of high risk patients

- Use of available patient education material
  - “Managing acute pain” MC 7643
Discharge Considerations

• Provide taper instructions as needed

Discharge Considerations

- Prescription quantity considerations:
  - Use opioid prescription monitoring program
  - Ensure disposal instruction and recommendations
    - FDA: FLUSH opioids
  - Modify “standardized” quantities as needed
    - 3-7 days should be sufficient

Dowell D et al. CDC Recommendations and Reports/March 18, 2016/65(1);1–49.
Self-Assessment Question #3

Surgery is a primary risk factor for prolonged opioid use.

True

False
Summary

- Multi-modal approach optimizes pain control in acute pain of surgical patients

- Complex pain management patients require additional therapy considerations to optimize their pain control in the post-operative period

- Surgery is not a primary risk factors for prolonged opioid use but post-operative clinical diligence is needed
Questions & Discussion

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References

References

• Dowell D. CDC Guideline for Prescribing Opioids for Chronic Pain — United States, 2016. Recommendations and Reports/March 18, 2016/65(1);1–49.