Pain Management Update

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Co-Founder San Diego Orthopedic Trauma Fellowship

DISCLOSURES

• Consultant
  – Mallinckrodt Pharmaceuticals
  – Pacira Pharmaceuticals
“The abuse of opioids...has a devastating impact on public health and safety in this country1,

1. First lifetime exposure to opioids may be when they are prescribed for postsurgical pain2
2. Leftover opioids prescribed for postsurgical pain can be misused and abused4

Initiation of Short-term Opioid Therapy in the Acute Setting May Lead to Long-term Use

A high potential for misuse, dependency, or diversion starts in the acute care postsurgical setting

Retrospective Cervical Spine Study1
Approximately one-third of all patients were still using opioids 1 year later
- 29% of patients who did not use opioids before surgery were still using opioids

Prospective Study Upper Extremity Surgical Procedures2
Virtually all patients received a postoperative analgesic prescription for 30 tablets
- On average, 29 tablets per prescription were not consumed, resulting in a total of 4639 leftover opioid pills

Our Children at Risk

A Longitudinal Examination of Medical Use and Misuse of Opioid Medication among Adolescent Sports Participants

1540 adolescents participated in three waves of data collection occurring between the 2009–2010 and 2011–2012 school years, with 83% of the baseline sample completing all three waves.

Adolescent males who participated in organized sports compared with those not involved in organized sports had
- Two times the risk of being prescribed an opioid medication (ie, medical use)
- 10-fold higher odds of medical misuse of opioid medication as a result of taking too much
- Four-fold higher odds of medical misuse of opioid medication to get high

Prescription Opioid Abuse: A Gateway to Heroin Use, Overdose, and Death

- The number of individuals reporting past-year heroin use almost doubled between 2007 (373,000) and 2012 (669,000).
- This increase "may be linked to PO users who transition...to heroin use, with PO use providing the entryway to regular opioid use, and ultimately, heroin injection."
- In 2014, 728 Virginians died from opioid-related drug overdoses compared to 700 highway fatalities.

Opioids Remain the Cornerstone of Postsurgical Pain Management

A study of 26 hospitals in the Southeastern US from January 2009 to December 2010 found that 36,529 of eligible adult (≥18 years of age) surgical patients (98.6%) received postsurgical opioids.

- In 2009, hydrocodone was the single most prescribed medication in the US.
- The CDC estimates that enough prescription painkillers were prescribed in 2010 to medicate every American adult around the clock for a month.

Department of Justice
U.S. Attorney's Office
Middle District of Georgia

FOR IMMEDIATE RELEASE
Friday, September 16, 2016

Prescription Opioid and Heroin Awareness Week
September 19-26, 2016

Attorney General Loretta Lynch has designated the week of September 19-23, 2016 as Prescription Opioid and Heroin Awareness Week. The prescription opioid and heroin epidemic has taken a heartbreaking toll on too many Americans and their families, while straining resources of law enforcement and treatment programs.
Acute perioperative pain

- Perioperative pain
  - Approximately 51 million inpatient procedures and 54 million outpatient surgeries are performed annually in the US.
  - Despite new treatment standards, guidelines, and educational efforts, acute post-op pain continues to be undertreated, with up to 75% of patients in the US still failing to receive adequate post-op pain relief.
  - The identification and management of pain is an important component of patient-centered care. Patients can expect their healthcare providers will involve them in their assessment and management of pain.
  - With the advent of Hospital Consumer Assessment of Healthcare Providers and Systems (HCAHPS) surveys, patients are now able to make decisions on hospitals based on quality of care, including quality of pain management.

Focus of HCAHPS on pain and patient satisfaction

- Pain
  - Establishing and maintaining an institutional pain performance improvement plan is a requirement of The Joint Commission.
- Patient satisfaction
  - Local, regional, or national patient satisfaction data are now being reported via HCAHPS (also known as CAHPS hospital surveys).
  - As part of the Affordable Care Act, the Centers for Medicare and Medicaid have established hospital reimbursement based on HCAHPS scores.
- Effective beginning October 1, 2012
A Multimodal Approach Uses a Variety of Therapeutic Agents to Minimize Opioid Use and ORADEs

Simultaneous use of a combination of ≥2 analgesics that act at different sites within the central and peripheral nervous systems in an effort to:
- Reduce pain
- Minimize opioid use and ORADEs

ORADEs = opioid-related adverse drug events.


COX-2 = cyclooxygenase-2; NMDA = N-methyl-D-aspartate; NSAIDs = nonsteroidal anti-inflammatory drugs.
Multimodal Strategies Support an Opioid-sparing Approach to Acute Pain Management

Traditional Approach
- Give More Opioids
- Breakthrough Pain
- Opioid

Multimodal Approach
- Neuraxial Analgesia
- Analgesics: Acetaminophen, NSAIDs, COX-2 inhibitors, Gabapentinoids, Local Anesthetics
- Breakthrough Pain
- Moderate to Severe Pain

COX-2 = cyclooxygenase-2; NSAID = non-steroidal anti-inflammatory drug.

Newly Adopted Multimodal Pain Management Strategy

Preoperative Period
- Patient education
  - Video and booklet
- Total joints boot camp
- Preanesthesia testing clinic education
- Preemptive analgesia
  - Acetaminophen
  - Gabapentin
  - Celecoxib

Intraoperative Period
- Ketorolac
- Liposomal bupivacaine
- Dexmedetomidine
- Opioid-tolerant patients
  - Ketamine
  - Clonidine

Postoperative Period
- Scheduled acetaminophen, gabapentin, and NSAIDs/COX-2 inhibitors
Complementary and Alternative Medicine (CAM) Approaches

Four of the top five conditions that use CAM approaches most often are chronic pain conditions associated with the back, neck, joints, and arthritis.

- Cognitive behavioral modalities: positive imagery or music therapy
- Ice, elevation, compression
- Deep breathing
- Heating pad
- Aromatherapy

Patient education is the biggest thing we can do to help!


Non-opioid Agents Administered as Part of Multimodal Analgesia

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose Before Surgery</th>
<th>Route of Administration</th>
<th>Time Before Surgery</th>
<th>After Surgery</th>
</tr>
</thead>
<tbody>
<tr>
<td>NSAIDs*</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ketorolac</td>
<td>15–30 mg</td>
<td>PO/IV</td>
<td>1–2 h</td>
<td></td>
</tr>
<tr>
<td>COX-2 Inhibitors*</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Celecoxib</td>
<td>400 mg</td>
<td>PO</td>
<td>1 h</td>
<td>15–30 mg qdh</td>
</tr>
<tr>
<td>Anticonvulsants**</td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Gabapentin</td>
<td>1200 mg</td>
<td>PO</td>
<td>1–2 h</td>
<td>1200 mg qd</td>
</tr>
<tr>
<td>Pregabalin</td>
<td>150 mg</td>
<td>PO</td>
<td>1 h</td>
<td>150 mg qd</td>
</tr>
<tr>
<td>Propacetamol</td>
<td>2 g</td>
<td>PO/IV</td>
<td>15 min</td>
<td>2 g q4h</td>
</tr>
<tr>
<td>Acetaminophen</td>
<td>1 g</td>
<td>PO/IV</td>
<td>15 min</td>
<td>1 g q4h</td>
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<tr>
<td>Liposomal Bupivacaine</td>
<td>Up to 266 mg</td>
<td>Injection into soft tissue of surgical site during surgery</td>
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</table>

Please see important safety information on slide 97. Full prescribing information is available at www.EXPARL.com.

Opioid Reduction with Multimodal Analgesia in TKA

Dexamethasone* 41%
NSAIDs* 15%–55%
Gabapentinoids** 10%–49%
Ketamine* 10%–30%
IV acetaminophen* Average reduction of 9 mg of morphine equivalents

TKA=total knee arthroplasty

Implementation of Hip Fracture Pain Management

• Complications of opioids include:
  – Alterations in mental status
  – Nausea and vomiting
  – Respiratory depression
  – Tolerance
• Which alternative or adjunctive methods are safe and effective options that can be used within the clinical circumstances of older adults with hip fracture?

Clinical Questions Addressed by the Comparative Effectiveness Reviews (CER)

• In older adults, what is the effectiveness of pain management interventions for controlling acute (up to 30 days postfracture) and chronic pain (up to 1 year postfracture), compared to usual care or other interventions?
• What is the effect of pain management interventions on outcomes other than pain (up to 1 year postfracture), compared to usual care of other interventions?
  – For example: mortality, mental status

Methods

• All citations generated from electronic or hand searching and expert nominated studies were pooled into a single database.
• Of these 9,357 citations retrieved, 2,241 were duplicates and 7,116 were considered to be unique study reports.
• Following level 1 screening, 6,496 were excluded and 620 were further evaluated for inclusion.
• Of these, 83 primary publications passed level 2 screening and were included in this Comparative Effectiveness Review.
• An additional 15 companion publications were identified and also included.
**Pain Management Interventions Included in this CER**

- **Systemic Analgesia**
  - Both narcotic (opioids) and non-narcotic (NSAIDs, acetaminophen) medications are typical in “usual care.”

- **Nerve Blocks (regional blocks)**
  - Injection of anesthetics into nerve bundles prevents the generation and conduction of nerve impulses to the spinal cord and brain.

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**Pain Management Interventions Included in this CER**

- **Traction**
  - A traditional approach for the population of patients with hip fracture.
  - Preoperative skin or skeletal traction.
  - Goal is to stabilize the fractured leg, to reduce pain, and to improve fracture reduction.

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**Pain Management Interventions Included in this CER**

- **Anesthesia**
  - Neuraxial: spinal and epidural
  - Injection of anesthetic into the epidural or subarachnoid space in the spinal column

- **Transcutaneous Electrical Neurostimulation (TENS)**
  - Applies electrical energy to peripheral nerves, to reduce the perception of pain
  - Uses varying amplitudes and frequencies, depending on indication
Pain Management Interventions Included in this CER

- Complementary and Alternative Medicine (CAM)
  - Systems, practices, and products that are not part of conventional medicine, such as:
    - Acupressure: applying pressure at body sites away from the pain locale.
    - Jacobson relaxation technique: alternating between contracting and relaxing muscles.
- Multimodal Pain Management
  - The use of multiple strategies as part of the clinical pathway.
  - Intent is to decrease pain to a greater extent than with one intervention alone

Summary of Benefits (1)

- Nerve Blocks
  - Reduce the intensity of acute pain
    - Strength of Evidence: moderate
  - Can be as effective as spinal anesthesia for relief of acute pain
    - Strength of Evidence: low
  - Reduce the likelihood of delirium (NNT=9)
    - Strength of Evidence: moderate
  - Do not affect mortality rates.
    - Strength of Evidence: low

Summary of Benefits (2)

- Spinal Anesthesia
  - Continuous versus single-dose modes do not differ in effect on mortality rates or incidence of delirium
    - Strength of Evidence: low
  - The evidence is insufficient to understand the effectiveness and benefits of differing doses, modes of administration, and the addition of opioids to the anesthetic injection.
- Skin Traction
  - Does not reduce the intensity of acute pain
    - Strength of Evidence: low
Summary of Benefits (3)

• Rehabilitation, Acupressure, Jacobson Relaxation Technique, and TENS:
  – The current evidence indicates that these modalities show some promise for pain relief, but the data are too limited to permit conclusions about the benefits or harms.

Conclusions About Benefits and Adverse Events

• Overall, there is limited evidence about the comparative effectiveness, benefits, and harms of pain management interventions used for elderly patients with hip fracture.
• Evidence of moderate strength supports the findings that nerve blocks reduce pain and the incidence of delirium when compared with usual care alone.

Conclusions About Benefits and Adverse Events

• Evidence of low strength supports finding that preoperative traction does not improve relief from acute pain.
• For all modalities, including those most commonly used (acetaminophen, NSAIDs, and opioids), the evidence is inadequate to estimate harms and the incidence of common adverse events in elderly patients with hip fracture.
Who Are the Decision Makers and What Are Their Concerns?

- Surgeons
- Anesthesiologists
- Pain Management Specialists
- Pharmacists
- Nurses
- Physical/Occupational Therapists
- Case Management Specialists
- Vice President of Perioperative Services

- "Don’t tell me how to treat my patient’s pain"
- "Doesn’t anesthesia handle all that?"
- "Who decides?"
- "Are they (e.g., peripheral nerve catheters/epidurals) still needed?"

Administration of Quantitative Assessments at Regular Intervals Can Help Determine Response to Treatment

- Numerical rating scales
- Functional pain scales
- Wong-Baker Faces Pain Rating Scale

**Newly Adopted Multimodal Pain Management Strategy**

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*EXPAREL® (bupivacaine liposome injectable suspension), Pacira Pharmaceuticals, Inc.
†Please see Important Safety Information at the conclusion of this presentation.

*Please see Important Safety Information on slide 116. Full Prescribing Information is available at EXPAREL.com.
Perioperative Opioid Program

Antimicrobial Stewardship

Venous Thromboembolism (VTE) Risk Assessment

Work Flow for Addiction Risk Assessment

BDNF = brain-derived neurotrophic factor; OPRM1 = opioid receptor mu 1; SOAPP = Screener and Opioid Assessment for Patients with Pain®.
Disease Gene Mutation Outcome

**Addiction**

- **BDNF Val66Met**
  - Associated with neurotransmitter dysfunction that increases the likelihood of drug abuse

- **DRD2 Taq1A**
  - Changes the brain's response to dopamine, a neurotransmitter that regulates reward and behavior, and leads to increased predisposition for drug abuse

- **OPRM1 Pro319Pro**
  - Associated with an extreme targeted response to opiate, and an impaired response to naltrexone

**Addiction Risk Screening**

**Sample Processing and Reporting**

PharmD reviews reports and provides perioperative management summary

**Enhanced Recovery After Surgery (ERAS) Are Multidisciplinary Perioperative Care Pathways**

- ERAS emerged in the mid-1990s as “fast-track surgery,” a concept developed by Henrik Kehlet, MD
  - Multimodal, evidence-based model initially developed for colorectal surgical care pathways
  - ERAS pathways accelerate postoperative recovery and reduce general morbidity by simultaneously applying multiple interventions based on evidence1,2
  - ERAS is designed to:
    - Attenuate the patient stress3
    - Maintain preoperative bodily compositions and organ function3
    - Integrate throughout the perioperative pathways4
    - Maintain physiologic functions3
    - Facilitate (early) postoperative recovery5
    - Reduce complications and LOS
    - Reduce variability
    - Increase value by reducing cost and improving quality of care6,7

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CDC 2016

- The Centers for Disease Control and Prevention (CDC) released prescribing guidelines for opioids on March 18, 2016
- The CDC guidelines state that
  - Non-pharmacologic therapy and non-opioid pharmacologic therapy are preferred for chronic pain
  - Long-term opioid use often begins with treatment of acute pain
  - Clinicians should prescribe the lowest effective dosage
  - Acute pain can often be managed without opioids

The CDC believes that **three days or less will often be sufficient for all persons**, and that more than seven days will rarely be needed

What Is California Doing?

- Partnership HealthPlan of California* launched the Managing Pain Safely Immediate Release Initiative June 1, 20161
  - New patients will be limited to 30 tablets of short-acting opioids in a 90-day time frame for an acute pain episode without prior authorization
- Beginning in 2013, the California Department of Health Care Services followed a three-pronged approach to improve opioid safety2:
  - Promotion of safe opioid prescribing
  - Naloxone distribution
  - Access to substance abuse treatment

What Is California Doing? (cont’d)

- The State of California Department of Justice’s Prescription Drug Monitoring Program is administering the Controlled Substance Utilization Review and Evaluation System (CURES)
  - The CURES Fund assesses an annual fee of six dollars ($6) for prescribers of controlled substances, wholesalers of dangerous drugs, non-governmental clinics, and pharmacies to support ongoing operation of CURES and improvements to CURES
  - All prescribers and dispensers of controlled substances and pharmacists are required to register for access to CURES before July 1, 2016
  - An update to CURES, CURES 2.0, is currently underway to streamline the application and approval process, improve the user interface, ease its use, provide a more robust analytic and reporting engine, and provide authorized users with information about at-risk prescription behavior
Thank You.