Multi-modal Pain Management in Foot and Ankle Surgery

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Peri-operative Goals in Foot and Ankle Surgery

• Minimize pain
• Minimize complications
• Maximize early and late recovery

Keys to a Successful Surgery

Good surgical technique
Rehabilitation & Education
Rapid Recovery
Pain Management
Mechanism of Surgical Pain

- Surgery activates the nociceptor system\(^1\(^{-2}\)
  - Central nervous system (CNS)
  - Peripheral nervous system
    - A delta (A\(\delta\)) fibers
      - Myelinated
      - Rapid transmission to CNS
      - Mechanical and thermal stimuli
    - C fibers
      - Unmyelinated
      - Mechanical, chemical, cold stimuli
      - Involved in inflammation


Mechanism of Surgical Pain

- Secondary inflammation
- Tissue damage
  - Inflammatory mediators/cytokines
- Reduction in pain threshold of nociceptor afferent nerves
- Hyperalgesia
  - Primary – injured tissue
  - Secondary – noninjured tissue
- Sensitization
  - Peripheral – inflammation
  - Central – repeated stimuli


Background

- More than 90 million procedures performed in the U.S. each year\(^1\(^{-2}\)
- 35 million ambulatory
- 56 million in-patient\(^1\(^{-2}\)
  - Orthopedic patients had the highest incidence of pain compared to other types of operations
  - >50% experience suboptimal pain control

Pain Management

**Physicians**
- Perioperative "hassle"
- Impaired rehabilitation
- Compromised outcomes
- Chronic pain
- Complications

**Patients**
- Fear
- Dissatisfaction
- Complex physiology
- Increased morbidity
- Hindered physiotherapy
- Increased anxiety
- Disrupted sleep
- Prolonged recovery

LOS = length of hospital stay.


Hospitals
- "5th vital sign"
- Prolonged LOS
- Quality measure

Joint Commission: "...patients have a right to adequate pain management"1

Health Economics
- Prolonged LOS
- Prolonged recovery
- Disability
- Medication side effects

How To Improve Our Outcomes Following Surgery?
- Patient expectations
  - Age, motion, activity
- Management of these expectations
  - Pre-operative
  - Peri-operative
  - Post-operative
- Multimodal pain control
- Rapid recovery, rehabilitation
Develop A Team & A Pathway

- Everyone on same page
  - Physician extenders, Office, Hospital, Home
- Be a “coach” to the patient
  - Instill confidence
- Explain upcoming experience
  - Expectation of pain in preoperative setting is related to amount of pain postoperatively

Remember: Postoperative Pain is #1 Patient concern

- Orthopedic procedures are among the most painful
- Up to 20% of pts can have pain at 1 yr
- Pain is the most common reason for fear/avoidance of surgery

↑Post-Op Pain = ↑Complications

- Prolonged hospital/rehab stay
  - (Kessler, et al, Morrison, et al)
- Elevated readmission rate
  - (Coley, et al)
- Higher Costs
  - (Oderda, Pogatzki-Zahn, et al)
- Postop pain control and rapid rehab protocols correlate with quality of recovery
Pain Management (2000s)

- Opioid analgesics were the cornerstone of post-operative analgesia following orthopedic surgery
  - Intra-op narcotics
  - IV narcotics
  - IM narcotics
  - PCA pumps
  - Oral long- and short-acting narcotics

Opioids Were The Conventional Approach

- Opioids (PO or PCA/IV) as the sole source of analgesia are associated with significant issues
- Opioid-related adverse events occur more frequently with:
  - Increased age
  - Obesity
  - Chronic COPD
  - Hepatic and/or renal impairment

Opioid-Related Adverse Effects

- Allergy
- Arrhythmias
- CNS adverse events
- Constipation
- Cough
- Dry mouth
- Endocrinopathy
- Histamine release
- Nausea
- Immunomodulation
- Increased intracranial pressure
- Myoclonus
- Nausea and vomiting
- Neurotoxicity
- Pruritus
- Respiratory depression
- Rigidity
- Santorini syndrome
- Urinary retention
- Withdrawal symptoms

Effect of Opioid-related Adverse Events on Outcomes

- 319,898 surgeries
- 12.2% patients experienced ORAE
  - Patients had higher adjusted mean costs:
    - $22,077 vs $17,370 (p <0.0001)
  - Greater LOS:
    - 7.6 vs 4.2 days (p <0.0001)
  - More likely to be readmitted (OR 1.06)

ORAE=opioid-related adverse events

Opioid Epidemic

White House Summit on the Opioid Epidemic:
“...has a devastating impact on public health and safety in this country”

- Each day, 46 people die from an overdose of prescription painkillers in the US
- HCPs wrote 259 million prescriptions for painkillers in 2012, enough for every American adult to have a bottle of pills
- 18 of the highest prescribing states are in the South

Hospitalizations and Emergency Department Visits Due to Opioid Overuse/Misuse Continue to Rise

- Between 2002 and 2012, hospitalization rates for opioid overuse among adults 21-8 years increased by >60%, with 709,500 opioid-related hospitalizations in 2012
  - The highest rate is currently in individuals aged 45-64 years
- Between 2006 and 2010, emergency department visits involving non-medical use of POs increased 15% (from 84,671 to 172,737)
Opioid Abuse Results in High Healthcare Costs

- Administrative database of medical and pharmacy claims from 1998-2002
- Patients with claims associated with codes for opioid abuse were identified; a control group of non-abusers was selected using a matched sample in a 3:1 ratio

![Graph showing healthcare costs](image)

Average Annual Direct Costs* of Opioid Abusers and Non-abusers, 1998-2002

<table>
<thead>
<tr>
<th>Category</th>
<th>Opioid Abusers</th>
<th>Non-abusers</th>
</tr>
</thead>
<tbody>
<tr>
<td>Other costs</td>
<td>$2034 (13%)</td>
<td>$386 (21%)</td>
</tr>
<tr>
<td>Physician’s visit/outpatient costs</td>
<td>$7659 (48%)</td>
<td>$318 (17%)</td>
</tr>
<tr>
<td>Hospital inpatient costs</td>
<td>$5398 (34%)</td>
<td>$928 (51%)</td>
</tr>
<tr>
<td>Drug costs</td>
<td>$793 (5%)</td>
<td>$198 (11%)</td>
</tr>
</tbody>
</table>

Total Direct Cost: $15,884

Total Direct Cost: $1830

Recent Gains in Knowledge: Multimodal Pain Management

- Minimize use of narcotics
  - Eliminate parenteral narcotics
- Decrease pain scores
- Decrease adverse side effects
- Increase patient satisfaction
- Decrease times to reach PT milestones

- Surgeon, pain management team compliance
- Well tolerated by patients

Effective Pain Control Requires a Combined Drug Synergy Effect

- Block generation and perception of pain at several different stages in pathway
- Stop pain before it starts
  - Neuraxial/Regional anesth
- Multimodal analgesia
  - Potentiate effect of each treatment individually
A Multimodal Approach Uses a Variety of Therapeutics That Work at Different Sites

- 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 ORAEs


A Multimodal Approach Is Recommended From Preoperative Stage to Discharge

PREOPERATIVE (Preemptive)1-6
- NSAIDs/COX-2
- Long-acting narcotic
- Acetaminophen
- Dexamethasone

INTRAOPERATIVE (Preemptive and Multimodal)2,5-8
- Regional anesthesia
- Peripheral nerve blocks
- Periarticular injections

POSTOPERATIVE (on schedule) (Multimodal)3,5,6,8
- Acetaminophen
- NSAID (COX-2)
- Narcotic (ATC vs breakthrough PRN)

DISCHARGE2,5,6
- Acetaminophen
- NSAIDs (COX-2)
- Narcotic
- Combinations

Preoperative Medications: Prevent/Minimize Initiation of Pain

- Oxycontin
  - Acts in dorsal ganglia and centrally
  - 10mg am pre-op

ATC = around-the-clock; COX-2 = cyclooxygenase-2; NSAID = nonsteroidal anti-inflammatory drug; PRN = taken as needed.
Preoperative Medications:
Prevent/Minimize Initiation of Pain

- Acetaminophen
  - 1000mg am pre-op
  - Central inhibitory effect
  - 1g PO/IV upon induction
  - 1g 4 hrs post-op

**Acetaminophen**
Mechanism and Efficacy in Multimodal Therapy

- Acts as a central analgesic
- ASA guidelines suggest around-the-clock acetaminophen be considered part of multimodal pain management
- Reduced use of opioids and requests for rescue medication over the first 24 hours post operation

ASA = American Society of Anesthesiologists; IV = intravenous; RCT = randomized, controlled trial.

Preoperative Medications:
Prevent/Minimize Initiation of Pain

- Celebrex 200/400 mg x 1 am pre-op
  - Inhibits peripheral nerve stimulation and central brain inflammatory and pain perception
  - Reduce IL-6 and PGE-2 intraarticularly
  - No increase bleeding risks, opioid use
  - ? Use in bony fusion cases

Meunier et al., Acta Orthop 2009, 2007; Reuben et al., Anesth Analg 2008; O'Connor & Lysz, Drugs Today (Barc) 2008; Huang et al., BMC Musculoskelet Disord 2008
Benefit of Selective NSAIDs
Mechanism and Efficacy in Multimodal Therapy

- NSAIDs inhibit activity of the COX enzymes to limit prostaglandin production
- Meta-analysis of 60 trials to determine whether NSAIDs, COX-2 inhibitors, or acetaminophen were better at reducing morphine consumption in the postoperative setting
- Affect on bony healing?

<table>
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<tr>
<th>Comparison</th>
<th>Mean Difference in Morphine Consumption Adjusted for Baseline Morphine Consumption, mg (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>NSAID vs Acetaminophen</td>
<td>-0.77 (-3.75, 2.21)</td>
</tr>
<tr>
<td>COX-2 vs Acetaminophen</td>
<td>-1.99 (-5.24, 1.24)</td>
</tr>
<tr>
<td>COX-2 vs NSAID</td>
<td>-1.22 (-3.43, 1.00)</td>
</tr>
</tbody>
</table>

CI = confidence interval; COX-2 = cyclooxygenase-2; NSAID = nonsteroidal anti-inflammatory drug; PCA = patient-controlled analgesia; PONV = postoperative nausea and vomiting.


Preoperative Medications:
Prevent/Minimize Initiation of Pain

- Gabapentin, pregabalin
- 300 mg or 75 mg x 1 am pre-op
- Inhibit transmission of pain in the dorsal ganglia of spinal cord
  - Decrease excitatory signal release along afferent pathway
  - Decrease glutamate (excitatory amino acid) and substance P release

Dexamethasone
Mechanism and Efficacy in Multimodal Therapy

- Dexamethasone reduces inflammation and tissue damage
- Meta-analysis of 45 studies
  - 6 mg dose most common
  - Administered preoperatively in 28/45 studies
  - Significantly reduced VAS pain scores at 2, 24 hours
  - Reduced opioid consumption at 2 and 24 hours
  - No delayed wound healing or infection
  - Increased blood glucose observed at 24 hours
  - Anti-nausea agent

VAS = Visual Analog Scale.

Peri-operative

• Good surgical technique
  – Minimally invasive
  – Minimize tissue trauma

• Minimize blood loss, transfusion rate
  – Tranexamic acid
  – IV, topical, oral, 50% ↓ blood loss
  – 1g IV upon induction; +/- 1g at end
  – You bleed less, it hurts less


Nausea/Vomiting Prevention

• Pre-emptive
  – Minimize narcotics
  – Zofran 4mg IV at induction, then prn
  – Scopolamine patch (h/o motion sick, nausea)
  – Hydration
  – Decadron 6-10 mg induction; +/- POD1

• Treatment
  – Reglan
  – Hydration

Regional Anesthesia

• Single shot spinal
  – Lower rates of cognitive dysfunction
  – Lower mortality (THA)
  – Lower mortality and LOS (TJA)
  – 11% neuraxial
  – 14.2% combined
  – 74.8% general
  – Bupivacaine (avoid duramorph)

Nerve Blocks

- Decrease nociceptive input and nerve hyper-excitability to decrease pain
- Blocks
  - Popliteal nerve
  - Saphenous nerve
  - Ankle block
    - Works best when separate block room available: efficient for surgeon

Peri-articular Injections (PAI)

- Local anesthetic
- NSAID
- Clonidine
- Epinephrine
- Antibiotic
- Steroid

Peri-articular Injections (PAI)

- Literature review of 21 and 29 RCT in TJA
  - Peri-articular injections
    - Better pain relief
    - Lower opioid consumption
    - Better ROM
    - Less nausea and vomiting
    - No difference in LOS


Peri-articular Injections (PAI)

- **Kim et al., FAI 2011, 60 feet**
  - HV osteotomy, inpatient, spinal
  - Ropivacaine, morphine, ketorolac, epi
  - Periosteum, deep soft tissues, subQ
  - Significantly less pain at 4 hrs → POD 1, safe
- **Gadek et al., FAI 2015, 118 pts**
  - Distal 1st MT osteotomy for HV
  - Spinal + bupiv/lido, postop IV ketoprofen, tylenol
  - Decreased pain for 1st 24 hours

Liposomal Bupivacaine

- Indicated for single-dose administration into the surgical site to produce postsurgical analgesia
- Deliver therapeutic levels of bupivacaine over 72 hrs
- Reduce opioid need w/o catheters or pumps

Pharmacokinetics Demonstrate Plasma Levels of Bupivacaine That Can Persist for 96 Hours

- Initial peak due to 3% extraliposomal bupivacaine
- Second peak due to slow release of bupivacaine from DepoFoam

Plasma Bupivacaine Concentration (ng/mL)

- EXPAREL 266 mg
- Exp 0-2 hours
- Exp 24-48 hours
- Exp 96 hours

Presented at the 2009 International Anesthesia Research Society Annual Meeting; March 2009; San Diego.
**Absorption Profile** of Liposomal Bupivacaine vs Bupivacaine HCL

- Time Post dose (h)
- Mean Bupivacaine Plasma Concentration (ng/mL)
- After local infiltration administration in men undergoing inguinal hernia repair.


**Injection Instructions for PAI**

- Technique dependent
  - Inject slowly into multiple areas around the surgical site (min 25G)
  - Aspirate to minimize the risk of intravascular injection
  - Maximum dosage should not exceed 266 mg (1 vial)

**Statistically Significant Reduction in Cumulative Pain Scores at 24 Hours in Orthopedic Model (Bunionectomy)**

- Placebo EXPAREL 106 mg
- Fewer AEs reported with EXPAREL (59.8%) than with placebo

Liposomal Bupivacaine in Forefoot Surgery

- **Golf et al., Adv Therapy 2011**
- **193 pts, HV**
  - Greater percentage patients pain free out to 48hrs
  - Decreased time to first opioid use
  - Decreased total opioid consumption in first 24 hrs

Effective Option in Postsurgical Pain Management

<table>
<thead>
<tr>
<th>Primary Endpoint/Measures</th>
<th>Reduction in pain over extended time period</th>
<th>Total avoidance of opioid rescue</th>
<th>Reduced total consumption of opioid rescue</th>
<th>Delayed use of opioid rescue</th>
</tr>
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<tbody>
<tr>
<td></td>
<td><img src="image" alt="P&lt;0.001" /> <img src="image" alt="P=0.0005" /></td>
<td><img src="image" alt="P&lt;0.0001" /> <img src="image" alt="P=0.048" /></td>
<td><img src="image" alt="P&lt;0.0001" /> <img src="image" alt="P=0.007" /></td>
<td><img src="image" alt="P&lt;0.0001" /> <img src="image" alt="P=0.001" /></td>
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</tbody>
</table>

Opioid-Related Secondary Endpoints

Patient Satisfaction Secondary Endpoints

- Reduction in pain over extended time period: ![P<0.001](image) ![P=0.0005](image)
- Total avoidance of opioid rescue: ![P<0.0001](image) ![P=0.048](image)
- Reduced total consumption of opioid rescue: ![P<0.0001](image) ![P=0.007](image)
- Delayed use of opioid rescue: ![P<0.0001](image) ![P=0.001](image)

Patient satisfaction: ![P<0.001](image) ![P=0.06](image)

Liposomal Bupivacaine in Forefoot Surgery

- **Parekh et al., FAI 2015**
  - 20 pts, multiple forefoot procedures
  - 400mg Celecoxib preop, ankle block lido/marcaine
  - 20cc/266mg Exparel at conclusion
- Lower #narcotic pills POD1-2, lower pain scores POD1-4, decreased refills, no increase wounds
Liposomal Bupivacaine and Cost Savings

- Exparel cost per vial: $285
- Decrease LOS, decrease adverse events
- Bupivacaine via Elastomeric Pump (> $450)
- Opioids w/ IV PCA (> $500)
- Decreased need for peripheral nerve blocks
  - Eliminate anesthesia fees/tech or FTE
- Medicare cost per fall: $13,797-$20,450
- Steadman-Hawkins (SC): estimated savings $1735 per TKA (Hawkins, Improving Patient Outcomes Symposium, 3/22/13)

Post-op Analgesia: On a Schedule, Not PRN

- Acetaminophen: 650 mg 6a/12n/6p
- Celebrex: 200 mg PO bid x 10d (nonfusion)
- Gabapentin or pregabalin: 300mg or 75 mg qd
- Long acting opioid (oxycontin q12 x 4d)
- Short acting opioid (percocet prn)
  - NO PCA

Use of Specific Non-pain Medications

- Muscle spasms (cyclobenzaprine)
- Nerve irritation (gabapentin)
- Nausea (metoclopramide, scopal patch)
- Vomiting (ondansetron)
- Constipation (senna-docusate)
- Ice/cooling machines
Multi-modal Pain Management: Results are Dramatic

- Little or no pain
- VAS Pain scores 0-3
- Patients alert, oriented, appropriate
- POD #1 most are sitting reading, eating breakfast
- Fewer calls!!

Conclusions: Pain Management

- Many patients experience suboptimal pain control following orthopaedic procedures

Conclusions: Ideal Pain Management

- Synergistic effect of multiple meds together
  - Provide effective analgesia
  - Minimize opioid use and side effects
  - Hasten mobilization and recovery
  - Decrease length of stay, reduce complications of hospital stay and immobilization
  - Reduce rates of readmission
  - Improve patient satisfaction scores
Conclusions:
Pain Management and Rapid Recovery

- Multimodal pain management continues to evolve
  - Minimize narcotics at all costs!!
- Marketing
- Benefits for you and me: thankful patients who recover faster

Conclusions:
Pain Management and Rapid Recovery

- Patient-driven outcome/satisfaction ratings
  - THE Major factor in future of healthcare delivery
  - Surgery is only part of the solution
  - HCAHPS scores (CMS)
  - Healthgrades, etc
  - MD, Hospital re-imbursement by payers
  - Ultimately…Your salary and mine

Thank You For Your Attention