Non-Opioid Postoperative Pain Management

2020 California Association of Oral and Maxillofacial Surgeons Anesthesia Meeting
Brian Goo, DDS
Highland Hospital, University of the Pacific, Kaiser Oakland
Outline

- Opioid Epidemic
- What is Pain?
  - Categories
  - Physiology of Nociception
- Importance of Pain Management
- Pain Management Recommendations
- Non-opioid post-operative pain management
  - NSAIDs
  - Acetaminophen
  - Gabapentinoids
  - Local Anesthetics
Opioid Epidemic and Prescribing

Early 90s, American Pain Society declared pain as the fifth vital sign

- Opioid prescriptions went from 76 million in 1991 to 220 million in 2011

Table 1. Opioid Prescribing by Specialty and Volume, July 1, 2016–June 30, 2017

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<th>Specialty</th>
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<td>970,902</td>
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<tr>
<td>Dentist</td>
<td>153,647 (15.8)</td>
<td>18,091,864 (8.6)</td>
<td>117.7</td>
<td>33.8 (8.7, 111.5)</td>
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<td>Nurse practitioner</td>
<td>119,599 (12.3)</td>
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- 2016 AMA and AAFP removed pain as a vital sign
What is PAIN?

- Derives from Latin word “poena” meaning “penalty”

- “An unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage.”
  - International Association for the Study of Pain 2017

- Subjective sensation
Categories of Pain

- Duration
  - Acute Pain
  - Chronic Pain
- Origin
  - Nociceptive
    - Somatic pain (external)
    - Visceral pain (internal)
  - Neuropathic pain
  - Psychogenic pain
- Referred pain
- Phantom pain
Nociception

- Nociception = neural process of encoding noxious stimuli (body sensing pin prick)
- Responsible for acute post-op pain
Physiology of Pain

- Nociceptors
  - Free nerve endings at site of tissue damage
  - Convert injury to action potential
  - Afferent nerve fibers → Spinal cord (Dorsal horn)
  - A-delta and C-fibers (somatic pain)
  - Dorsal horn → Thalamus → Cortex
  - Ascending pathway - Spinothalamic tract

(Dureja, 2017)
Why is post-op pain management important?

- Slower recovery and rehabilitation
- Reduces quality of life
- Increases health care costs (ED visits for pain)
- Risk of pneumonia, DVT, post-operative cognitive dysfunction (inpatient setting)
- Not a good practice builder
AAOMS 2017 White Paper
Post-op Pain Management Recommendations

- Pre-emptive nonsteroidal anti-inflammatory
- Perioperative corticosteroid
- Long-acting local anesthetic
- Post-op analgesic medications
  - First line: NSAIDs vs. acetaminophen
  - Second line: opioids for breakthrough
- Educate patients
Post-op Pain Management Timeline

Initial Consult
- Patient education

Pre-op Interventions
- Tylenol
- Gabapentin
- Celebrex
- Clonidine

Intra-op
- Fentanyl
- Decadron
- Ketamine
- Local anesthetic

Post-op
- Immediate Post-op
- Discharge/Home
Non-Opioid Post-op Analgesics

- Nonsteroidal Anti-inflammatories (NSAIDs)
- COX-2 selective inhibitors
- Acetaminophen/Paracetamol (Tylenol)
- Gabapentinoids (Gabapentin, pregabalin)
- NMDA receptor antagonists (Ketamine)
- Local Anesthesia
**NSAIDs**

- **Use:** Analgesic, anti-inflammatory, antipyretic

- **MOA:**
  - nonselective inhibition of COX-1/COX-2
  - Selective inhibition of COX-2
  - Inhibit prostaglandin synthesis

- **Metabolism:** Hepatic

- **Adverse effects:**
  - GI upset/ulcers
  - Anti-platelet effect
  - Renal impairment
  - Heart failure - exacerbation
  - MI, stroke

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**Diagram:**

- **Surgical Stimulus (Injury to Cell Membrane):**
  - Membrane Phospholipids
    - Phospholipase A2
    - Corticosteroids
    - Arachidonic Acid
    - NSAIDS
      - Cox-1
      - Cox-2
      - Cox-2 Inhibitors
    - Lipoxygenase
      - Cytoprotective Prostanoids
        - Maintain normal physiology
        - Maintain healthy gastric mucosa
        - Maintain platelet aggregation
        - PGE2, Prostacyclin, Thromboxane A2
      - Inflammatory Prostanoids
        - Induced with tissue injury
        - Pain and tenderness
        - Vasodilation
        - Fever
      - Leukotrienes Lipoxins
        - Vasoconstriction/Vasodilation
        - Pain
        - Inflammation
        - Bronchial Constriction
        - Gastric Mucous Protection

Fletcher, 2002
Nonselective NSAIDs

- Salicylates
  - Aspirin

- Propionic Acid derivatives
  - Ibuprofen (Motrin, Advil)
  - Naproxen
  - Ketoprofen

- Acetic acid derivatives
  - Toradol - IV (the only IV NSAID available in US)
  - Diclofenac
  - Indomethacin
Toradol (Ketorolac)

- Indication: moderate to severe acute pain
- Route: IV, IM, PO (100% bioavailability)

<table>
<thead>
<tr>
<th>Route</th>
<th>Onset</th>
<th>Peak</th>
<th>Duration</th>
</tr>
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<tr>
<td>P.O.</td>
<td>1/2-1 hr</td>
<td>1/2-1 hr</td>
<td>6-8 hr</td>
</tr>
<tr>
<td>I.V.</td>
<td>Immediate</td>
<td>Immediate</td>
<td>6-8 hr</td>
</tr>
<tr>
<td>I.M.</td>
<td>10 min</td>
<td>1/2-1 hr</td>
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- Dosing: IV bolus 15-30mg every 6 hours maximum 5 days, or single immediate post-op dose
- Contraindications: prophylactic analgesia, pregnancy, bleeding risk, peptic ulcer disease, taking other NSAIDs, CV disease, renal impairment
“(1) Opioids are more efficacious than analgesics than NSAIDs…(2) adding NSAIDs to the opioid treatment reduces morphine requirements and opioid-related side effects in the early postoperative period.”

- Cepeda et al. 2005
Selective COX-2 inhibitors
Celecoxib (Celebrex)

- Osteoarthritis, rheumatoid arthritis, acute pain in adults
- PO 100mg BID or 200mg Qday
  - Extended half-life
  - Decreased frequency of dosing
- No affect on platelet aggregation
- Increased risk of CV events as compared to ibuprofen (Fletcher and Spera, 2012)
- Higher cost compared to ibuprofen
Cox-2 Selective NSAID:
- Increased risk for CV events
- Decreased risk for GI side effects

Meloxicam, diclofenac, etodolac, indomethacin, piroxicam, nabumetone, sulindac

Semiselective NSAIDs:
- Increased affinity for COX-2 but still retain activity for COX-1
- Use with caution in patients at increased CV risk

Ibuprofen, naproxen

Nonselective NSAIDs:
- Decreased risk for CV events
- Increased risk for GI side effects

Aspirin

Irreversible Nonselective NSAID:
- Cardioprotective at low doses
- Increased risk for GI side effects
Ibuprofen vs Celecoxib

Comparative Analgesic Effects of Ibuprofen, Celecoxib and Tramadol after third Molar Surgery: A Randomized Double Blind Controlled Trial.
Akinbade et al., Journal of Contemporary Dental Practice - Nov 2018

- Ibuprofen vs celecoxib vs tramadol after 3rd molar extractions
- 135 patient randomized into 3 drug groups
- Administered PO medications immediately after surgery to 48hrs post-op
- VAS used to record pain intensity at multiple time points

CONCLUSION:
- Celecoxib > Ibuprofen > Tramadol at 4 hrs (P=0.0039)
- Celecoxib had the lowest mean VAS at 4, 8, 24, and 48hrs
- NO adverse effects reported with celecoxib or ibuprofen group
Acetaminophen (Paracetamol, APAP)

- Antipyretic, analgesic (mild to moderate)
- MOA unclear
  - Crosses blood brain barrier
  - Inhibits prostaglandins via COX pathway
  - Cannabinoid receptors
  - Inhibits nitric oxide pathway
- Peak plasma concentration
  - PO - 45 to 60 minutes
  - IV - 15 minutes
- Adults: 1 gram every 4-6 hours, maximum 4g (2g for elderly, renal or hepatic impairment, regular alcohol use)
- Children <12yrs: 10-15mg/kg per dose, 5 doses/day
Intravenous versus Oral Acetaminophen for Pain: Systematic Review of Current Evidence to Support Clinical Decision-Making

Farah Jibril, Sherif Sharaby, Ahmed Mohamed, and Kyle J Wilby

- Literature search (PUBMED, Embase, IPA) from 1948-2014
- 6 RCTs reporting outcomes of efficacy, safety, and pharmacokinetics

CONCLUSION: For patients who can take an oral dosage form, no clear indication exists for preferential prescribing of IV acetaminophen.
Acetaminophen + NSAIDs

“Current evidence suggests that a combination of paracetamol and an NSAID may offer superior analgesia compared with either drug alone.”

- Ong et al., Anesthesia and Analgesia, 2010.

METHODS:
• Systematic Review
• Double blind RCTs between January 1988 to June 2009
• 21 studies, 1909 pts
• NSAIDS+paracetamol combo vs NSAID only or Paracetamol only

RESULTS:
Combo vs paracetamol                   Combo vs NSAIDs
- Mean reduction in pain intensity 35%  - Mean reduction in pain intensity 37.7%
Gabapentinoids (Gabapentin, Pregabalin)

- Anticonvulsant, analgesic (chronic neuropathy, acute pain?)
- Route: PO only
- Analogous in molecular structure to γ-aminobutyric acid (GABA)
- MOA: exact mechanism unknown, does not directly bind to GABA receptors
  - Inhibition of a2 subunit of voltage gated calcium channel, inhibits excitatory pathways
- Excretion: Renal
- Side effects: drowsiness, dizziness, visual disturbance, abuse potential
Systematic review results in 4 unpublished articles which met criteria of single dose, double blind, placebo controlled trials for moderate to severe postoperative pain relief in adults

CONCLUSION: “Gabapentin 250 mg is statistically superior to placebo in the treatment of established acute postoperative pain... but Gabapentin 250 mg is not clinically useful as a stand-alone analgesic in established acute postoperative pain.”
Local Anesthetics

- Lidocaine or bupivacaine nerve blocks and infiltrations
- Local injection of Ketamine
- Liposomal bupivacaine (Exparel) infiltrations
Ketamine

- **Use**: Anesthesia, analgesia, potential anti-inflammatory
- **Route**: IV, IM, SQ
- **MOA**: N-Methyl-d-aspartate (NMDA) receptor antagonist
- **Side Effects**: Hallucination
Local Ketamine Improves Postoperative Analgesia After Third Molar Surgery

Vicente Esparza-Villalpando DDS, MSc *, Ruben Ascencio-Padilla DDS †, Amaury Pozos-Guillen DDS, MSc, PhD ‡, Fernando Pozos-Guillen MD §§, Jose Antonio Hidalgo-Hurtado DDS l, Daniel Chavarria-Bolaños DDS, MSc, PhD ¶

► “The use of LAK (local administration of ketamine) can reduce the incidence and severity of postoperative pain after third molar surgery and had an anti-inflammatory effect, although only in the first postoperative day.

- Esparza-Villalpando et al., JOMS, 2019

► Analgesia - local + ketamine > local only

► Inflammation - local + ketamine significantly less swelling in the first postoperative day

► Trismus - no significant difference
Liposomal Bupivacaine (Exparel)

- “EXPAREL is indicated for single-dose infiltration in adults to produce postsurgical local analgesia and as an interscalene brachial plexus nerve block to produce postsurgical regional analgesia.” - Pacira Pharmaceuticals

- 1.3% Bupivacaine, encapsulated in multivesicular liposomes (Depofoam)

- Long lasting local anesthetic - up to 96 hours analgesia

- Cost: 133mg (10mL) vial $175, 266mg (20mL) vial $325

- Adverse effects similar to that of bupivacaine

Pacira Pharm, 2019
Injection Technique - Dr. Stuart Lieblich

**INFECTION AND NERVE BLOCK WITH NON-EXPAREL ANALGESICS**

**UPPER MOLARS**
- **Step #1**: Buccal and palatal infiltration of teeth #1 and #16 (lidocaine with epinephrine)

**LOWER MOLARS**
- **Step #2**: Inferior alveolar and lingual nerve block for teeth #17 and #32 (lidocaine with epinephrine)
- **Step #3**: Inferior alveolar and long buccal nerve block (bupivacaine HCl with epinephrine)

**INFECTION WITH EXPAREL**
- **Step #4**: Lateral aspect of mandible for teeth #17 and #32
- **Step #5**: Buccal aspect of teeth #1 and #16

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References


- Shah, Anand. (2016). Efficacy of Ketamine as an Adjunct to Local Anesthesia in the Surgical Removal of Impacted Mandibular Third Molars - A Split Mouth Prospective Controlled Clinical Study. JOURNAL OF CLINICAL AND DIAGNOSTIC RESEARCH. 10. 10.7860/JCDR/2016/19677.8638.
References

- Guy G, Zhang K. Opioid Prescribing by Specialty and Volume in the U.S. AJPM. Published online October 5, 2018. DOI: j.amepre.2018.06.008
- https://www.cdc.gov/drugoverdose/data/prescribing.html
- https://www.iasp-pain.org
- https://www.exparel.com/hcp/video/oral-maxillofacial/15/
- http://projects.hsl.wisc.edu/GME/PainManagement/session2.2.html - University of Wisconsin School of Medicine and Public Health
Thank you!
Special Populations

- **Pediatric**
  - No aspirin - Reye syndrome
  - Tylenol and Ibuprofen in weight based dosing
  - No codeine under age 12

- **Geriatric**
  - Kidney disease - caution with nsaids, decrease renal blood flow and GFR
  - Heart disease - acetaminophen, no nsaids or consider naproxen
  - Liver disease - cautious dosing of all drugs, acetaminophen is not contraindicated, caution with NSAIDS esp cirrhotics (coagulopathy)
  - Anticoagulated - Tylenol, tramadol, opioid