TRAUMA AND PAIN
“EXPLORING MULTIMODAL ANALGESIA”

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DISCLOSURES

OBJECTIVES

1. Discuss prevalence, costs, and impact of pain secondary to trauma in US population.
2. Understand basic pain physiology.
3. Understand rational behind multimodal analgesia
4. Appreciate range of options to meet post traumatic pain care needs.
UNIVERSITY OF WASHINGTON LEGACY
WHERE PAIN as a SPECIALTY BEGAN 1960

J.J. Bonica

INSTITUTE OF MEDICINE 2011 MANDATES
“TRANSFORMATION” OF PAIN CARE

Relieving Pain in America: A Blueprint for Transforming Prevention, Care, Education and Research, Institute of Medicine Report 2011

>100 Million
> 600$ Billion

Injuries Cost the U.S. $671 Billion in 2013

Over two thirds of these costs were due to nonfatal injuries

Nonfatal Injury $487 Billion
Fatal Injury $124 Billion

Injuries Cost the US $671 Billion in 2013 - Pie chart showing over two thirds of injury costs were due to nonfatal injuries.
TRAAUMA PAIN: UNIQUE TREATMENT CHALLENGES

- Acute pain can lead to changes in nervous system that result in chronic pain (neuroplasticity).
- Population comorbidities impacting pain care
- Multimodal balanced analgesia – when and what?
- Timeline
- High dose of opioids, worsening pain and acute tolerance (hyperalgesia)
- Treatment of acute postoperative pain in patients on chronic opioid therapy and those with opioid use disorders (OUDs)
- Safety issues – role in national opioid epidemic?

UNIQUE TREATMENT CHALLENGES

PHARMACOECONOMICS AND OUTCOMES IN PAIN AND PALLIATIVE CARE

Effect of Opioid-Related Adverse Events on Outcomes in Selected Surgical Patients

Cary M. Wible, Taj J. Esl, Benjamin H. Jibor, and From J. Hileman

ABSTRACT

ORADE

- Increased LOS
- Increased Cost

Increased LOS and increased cost of healthcare can have serious consequences for patients, providers, and payors. The purpose of our study was to assess the impact of the occurrence of opioid-related adverse events (ORAE) on hospital costs and length of stay (LOS) of surgical patients. We hypothesized that the rates of ORAE were significantly higher in patients with chronic opioid use, and that patients with ORAE were more likely to have increased LOS and increased costs. We conducted a retrospective cohort study of all adult patients treated at a major academic medical center from January 2010 to December 2012. Patients were identified as having ORAE if they met criteria for any of six adverse events: opioid overdose, opioid withdrawal, opioid-related death, opioid-related medication error, opioid-related allergy reaction, and opioid-related sedation or respiratory depression. Patients were considered to be chronic opioid users if they received opioid analgesics within 90 days of surgery. We compared the incidence of ORAE, LOS, and total charges between patients with and without chronic opioid use. We also compared the incidence of ORAE, LOS, and total charges between patients with and without an opioid-related adverse event. We used logistic regression to adjust for potential confounders. We found that patients with chronic opioid use were more likely to have ORAE, and that patients with ORAE had significantly increased LOS and increased charges. These findings suggest that efforts to prevent ORAE are necessary to improve patient outcomes and reduce healthcare costs.

Journal of Pain & Palliative Care Pharmacotherapy 2013
Drug Dealers Aren’t to Blame for the Heroin Boom. Doctors Are.

By Graeme Wood


Management of Postoperative Pain: Clinical Guidelines

APR, Skeene E. Amer, MD, PhD, MPH, ACHI BC
ASA, Cutler B., MD, ASA
HAA, Tanenbaum, Ed, DABPS
Society of Regional Anesthesiologists and Pain Medicine
American Society of Regional Anesthesiologists
American Society of Anesthesiologists

Journal of Pain Feb 2016


Final Recommendation Topics

- Preoperative education and perioperative pain management plans
- Methods of assessment
- Use of physical modalities
- Use of systematic pharmacological therapies
- Use of local/topical pharmacological therapies
- Use of peripheral regional anesthesia
- Use of neuraxial therapies
- Use of acute pain services
- Transitioning to outpatient care

MULTIMODAL ANALGESIA – WHAT IS IT?

“The use of a number of drugs, analgesic or adjuvant, in combination to achieve the best pain relief in acute or chronic pain will minimizing undesired side effects”

PRINCIPLES OF ACUTE PAIN - MULTIMODAL THERAPY
MULTIMODAL ANALGESIA – WHAT IS IT?

"Multimodal analgesia is readily available and the evidence is strong to support its efficacy. Surgeons should use this effective approach for patients both using and not using the ERAS pathway to reduce opioid consumption."

PRINCIPLES OF ACUTE PAIN - MULTIMODAL THERAPY

- Pain Pathways
  - Transduction
  - Transmission
  - Perception
  - Modulation

PRINCIPLES OF ACUTE PAIN - MULTIMODAL THERAPY

- Patient engagement
- Provides a way to achieve balanced, safer pain therapy
- Improved quality of analgesia
- Fewer side effects
- Better functional status

THE "PAIN EXPERIENCE" LOESER ONION

- **Nociception**: Nociceptors selectively respond to noxious stimulation.
- **Pain**: "Unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage" (IASP 1979).
- **Suffering**: Response to diminishment of one's capacity.
- **Behavior**: What we observe during exam of our patients.

PRINCIPLES OF ACUTE PAIN - MULTIMODAL THERAPY

"Recognize that each patient represents an individual therapeutic "experiment" that requires careful selection and titration of therapy."


ANALGESIC CLASSES

- **Nonopioids (acetaminophen, NSAIDs)**
- **Opioids**
- **Anticonvulsants**
- **Antidepressants**
- **Local anesthetics**
- **Alpha-2 agonists**

*NSAID = nonsteroidal anti-inflammatory drug.*
NSAIDS

- Aspirin the prototype: irreversible inhibitor
- Anti-inflammatory, antipyretic and analgesic effects, Affect uterine contractility
- Indicated for mild to moderate pain
- Principle mechanism of action is inhibition of prostaglandin synthesis
- Side effects depend partly on whether drugs are selective (COX-2) or nonselective
  - Impaired hemostasis (nonselective)
  - GI irritation/bleeding (nonselective)
  - Cardiovascular risk
  - Renal toxicity

Toradol (Ketorolac)

- Parenteral
- Extremely efficacious
- 30mg equivalent to 6-12mg parenteral morphine
- Many risks: stomach, kidneys, platelets
- Maximum 5 day therapy
- Reduced doses in patient >65 years, <50kg, renal insufficiency, or hypovolemia

ADVERSE EFFECTS OF NSAIDS

- GI tract – upper and lower gut: risk of GI bleed reduced 50% with a COX-2 inhibitor, but not if taking low dose aspirin
- Kidney – risk with both classes: fluid retention, increase in bp, renal failure
- “Hypersensitivity” reactions: aspirin-sensitive asthma with non-selective NSAIDs; skin rxs with coxibs
- Platelets – only nonselective (COX-1 inhibitors)
- CNS Effects – changes may be subtle
- Cardiac effects
CONTROVERSY WITH NSAIDS

- Contraindicated in CABG
- Observational data suggests possible association between high-dose NSAID and non-union in spinal fusion, but no clear association in other orthopedic surgeries
  - Prudent use appears reasonable option in selected patients at standard doses ≤ 14 days
- May increase risk of anastomotic leak in colorectal surgery
- Insufficient evidence to recommend against NSAIDS in fracture, spinal fusion or colorectal surgery but acknowledge uncertainty of harms


WHICH NSAID IS AVAILABLE FOR TOPICAL ADMINISTRATION?

A. Naproxen (Aleve)
B. Celecoxib (Celebrex)
C. Diclofenac (Voltaren)
D. Ketorolac (Toradol)

TOPICAL NSAIDS

- 1% diclofenac gel (Voltaren Gel®) – approved for treatment of OA pain
- Diclofenac patch (Flector®) – approved for treatment of pain due to minor strains, sprains and contusions
- Diclofenac topical solution (Pennsaid®): 1.5% diclofenac sodium solution in a carrier containing DMSO; available in Canada and Western Europe
- Aspercreme® – 10% trolamine salicylate
38% problematic alcohol use
44% positive urine for illicit drugs


Opioid: refers broadly to all compounds related to affecting opioid receptors
Narcotic: derived from the Greek word for stupor; once used for any drug that induced sleep; later associated with opioids; now used in a legal context to refer to drugs that are abused

Mu-agonists
- morphine, methadone, codeine, hydrocodone, fentanyl, oxycodone, oxymorphone
Partial mu-agonist antagonists
- buprenorphine
Mixed agonist antagonists
- nalbuphine, butorphanol, pentazocine
Central (mu + NE/5HT)
- tramadol, tapentadol
Antagonists: naloxone, naltrexone
**EXAMPLE: EQUIANALGESIC TABLE**

<table>
<thead>
<tr>
<th>Drug</th>
<th>Oral (mg)</th>
<th>Parenteral (mg)</th>
<th>Duration (hrs)</th>
</tr>
</thead>
<tbody>
<tr>
<td>morphine</td>
<td>30</td>
<td>10</td>
<td>3-4</td>
</tr>
<tr>
<td>hydromorphone</td>
<td>7.5</td>
<td>1.5</td>
<td>3-4</td>
</tr>
<tr>
<td>codeine</td>
<td>200</td>
<td>130</td>
<td>3-4</td>
</tr>
<tr>
<td>oxycodone</td>
<td>20-30</td>
<td>-</td>
<td>3-4</td>
</tr>
<tr>
<td>oxymorphone</td>
<td>10</td>
<td>1</td>
<td>4-6*</td>
</tr>
<tr>
<td>hydrocodone</td>
<td>30</td>
<td>-</td>
<td>3-4</td>
</tr>
<tr>
<td>meperidine</td>
<td>300</td>
<td>100</td>
<td>2-3</td>
</tr>
<tr>
<td>levorphanol</td>
<td>4</td>
<td>2</td>
<td>6-8</td>
</tr>
<tr>
<td>fentanyl</td>
<td>transdermal (TTS)</td>
<td>0.1</td>
<td>48-72 TTS 1-2 IV</td>
</tr>
<tr>
<td>methadone</td>
<td>10*</td>
<td>5*</td>
<td>6-8*</td>
</tr>
</tbody>
</table>

**DESIURABLE EFFECTS OF OPIOIDS**

- Effective analgesia
- Relief of anxiety
- Improved mood

**CORRELATION BETWEEN THERAPEUTIC EXPOSURE AND ABUSE**

*A heroin addiction can start in the most innocent of places, not under a bridge, but in the dentist’s chair or pediatrician’s office.*


OPIOID PRESCRIPTIONS AFTER SURGERY CAN LEAD TO LONG-TERM USE

In a retrospective study of patients undergoing elective surgery for repair of the Cervical Spine, at 1-year post surgery:
- Approximately one-third of all patients were still using opioids
- 18% of patients who did not use opioids before surgery were still using opioids

In a retrospective cohort study of older patients (>65 years of age) undergoing low-risk surgery and receiving an opioid prescription within 7 days of surgery:
- 10.3% were still taking opioids a year later
- There was a 44% increase in likelihood that they would become long-term opioid users, compared to patients not receiving a prescription

“...initiation of short-term opioid therapy may lead to their longer-term use”


OPIOID PRESCRIPTIONS AFTER SURGERY CAN LEAD TO LONG-TERM USE (CONT’D)

In a prospective, longitudinal inception cohort study in patients undergoing mastectomy, lumpectomy, thoracotomy, total knee replacement, or total hip replacement:
- 6% of patients continued on new opioids 150 days after surgery
- In addition to pain duration, increased risk was associated with non–pain-related factors
- If this 6% rate of long-term use were applied to the ~17.6 million people undergoing procedures, it would result in 1.1 million new “chronic” opioid users annually

“...there was a very strong correlation between therapeutic exposure to opioid analgesics... and their abuse”


NON-THERAPEUTIC ROLES

Richard Bowsfort-Mines
The Pursuit of Oblivion
A History of Narcotics 1940 - 1980
TACKLING THE POSTSURGICAL OPIOID

- Opioid-related adverse drug events (ORADEs) are a leading cause of preventable harm in hospitals.

- The Joint Commission issued a Sentinel Event Alert on "Safe use of opioids" and encouraged screening for risk factors.

- A variety of government organizations and organizations such as the ASA Task Force on Acute Pain Management recommend multimodal care and weighing risks and benefits of systemic opioids.

- First lifetime exposure to opioids may be when they are prescribed for postsurgical pain.

- Leftover opioids prescribed for postsurgical pain can be misused and abused.

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ADJUVANT MEDICATIONS

- Drugs with primary applications other than pain management
- Some are effective in certain painful conditions
- Adjuvant analgesics
  - Antidepressants
  - Anticonvulsants
  - Local Anesthetics
  - Alpha, adrenergic agonists
  - NMDA receptor antagonists
  - Corticosteroids and others
  - Muscle relaxants
  - Hypnotics and anxiolytics

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TRICYCLIC ANTIDEPRESSANTS

- Most studied, particularly for diabetic neuropathy pain
- Improvement of depression, insomnia
- Generally least well tolerated in elderly
- Start low, go slow, titrate slowly to effect or limiting side effects
- Large number of drugs: nortriptyline, desipramine
- Risk of conduction abnormalities: get baseline EKG

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SNRI: SELECTIVE NOREPINEPHRINE REUPTAKE INHIBITORS

- Fewer side effects than TCAs
- duloxetine (Cymbalta®)
  - First drug released for both depression and NP
  - Start: 30 mg a day; max 60 mg twice daily
- venlafaxine (Effexor®, Effexor XR®)
  - 37.5 mg once or twice daily; max 225 daily
- milnacipram (Savella®)
  - Approved for fibromyalgia

ANTICONVULSANTS / ANTIEPILEPTIC (AED)

- Decrease excitability of neurons by modulating voltage gate channels (sodium/calcium)
- Emerging as top-line adjunct in acute pain and first-line therapy in chronic pain
- Side effects/limitations
  - Most common side effects are CNS related, including sleepiness, dizziness, and fatigue

ANTIEPILEPTIC DRUGS

- First generation
  - Older drugs such as carbamazepine (Tegretol®) and phenytoin (Dilantin®)
- Second generation
  - A dozen have been released in the last fifteen years; gabapentin and now pregabalin most used
  - Greater tolerability, fewer drug-drug interactions, new mechanisms of action
GABAPENTIN AND PREGABALIN PERIOPERATIVELY

- > 43 RCTs and multiple systematic reviews
- Small reduction in pain in (acute hyperalgesia) pronociceptive models
  - Spine, arthroplasty, amputations
- Opioid sparing with single dose
  - 9-21%
  - Not gabapentin dose dependent
- Number-needed-to-harm 35 sedation/12 dizziness
- Dose defining study for gabapentin in diskectomy = 600mg (pregabalin ??150mg)

ANTICONVULSANTS: SIDE EFFECTS

- Clonazepam: drowsiness, ataxia
- Gabapentin: sedation, dizziness, nausea teratogenic
- Pregabalin: dizziness, sedation
- Carbamazepine: sedation, dizziness, nausea, unsteadiness, 2% leukopenia, thrombocytopenia
- Phenytoin: sedation, mental clouding, unsteadiness
- Valproic acid: sedation, nausea, tremor

PRINCIPLES OF ACUTE PAIN - MULTIMODAL THERAPY

"We found that most recently published clinical studies of gabapentinoids for pain examined single-dose or short-course gabapentinoids for mitigating postoperative pain, an indication that isn't relevant to general outpatient practice".

"Although gabapentinoids offer an advantage that is potentially worth pursuing and has not been shown to be overprescribed in outpatient settings, it is not clear that they are not overprescribed in our outpatient setting. The information on the internet is not clear and even through a thorough searching of references it is hard to find any clear guidance on the prescribing of gabapentinoids."

UW Medicine - PAIN MEDICINE
LOCAL ANESTHETICS

- Modulate sodium channels
- When administered peripherally, may produce differential—also known as sensory—block
  - Interrupts some nerve conduction, but leaves motor function unaffected
  - Some nerves are more readily blocked than others, depending on size and myelination
- Epidurally, interrupts pain input at the nerve roots
- Associated with few side effects

EPIDURAL LOCAL ANESTHETICS

<table>
<thead>
<tr>
<th>Function Blocked</th>
<th>Possible Problem</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sympathetic</td>
<td>Frank or orthostatic hypotension; Bradycardia (T1-T4 cardiac accelerators)</td>
</tr>
<tr>
<td>Proprioception</td>
<td>Difficulty ambulating</td>
</tr>
<tr>
<td>Sensory</td>
<td>Pressure injury; Mask a complication; Unable to self-void</td>
</tr>
<tr>
<td>Motor</td>
<td>Loss of motor function (ineffective cough, ambulation)</td>
</tr>
</tbody>
</table>

IV LIDOCAINE FOR VISCERAL SURGERY

- 8 RCTs: 6 open surgery, 2 laparoscopic
- Significant decreases
  - Duration of ileus
  - Length of hospital stay
  - Postoperative pain
  - Incidence of nausea and vomiting
- Attenuated levels of pro-inflammatory mediators
  (IL-6, IL-8, IL-1ra, complement C3a integrins, platelet leukocyte aggregates)
- Questionable benefit in spine surgery

**WHAT ABOUT KETAMINE?**

- N-Methyl-D-Aspartate (NMDA) Antagonist
- Activation of NMDA receptors has been associated with hyperalgesia, neuropathic pain, and reduced functionality of opioid receptors
- Does not cause respiratory depression at subanesthetic dosing
- Does not depress cardiovascular function, hepatic blood flow, nor bowel function
- Dissociative and amnesic
- Potential adverse CNS effects, e.g., bad dreams, hallucinations are mild and uncommon – dose related

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**Trauma: Pain Interventions**

- **Original Article**
  - Nurse-Led Psychological Intervention After Physical Traumas: A Randomized Controlled Trial
  - Laila Skogstad, Erlend Hem, Leiv Sandvik, Oivind Ekeberg

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**Trauma: Pain Interventions**

- RCT, 145 subjects, Impact of event score (IES) > 20
- Nurse delivered – 60 min structured cognitive behavioral therapy vs. CAU
- Reduce Posttraumatic symptoms at 1 year

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**Skogstad et. al., 2015**
LOW-QUALITY EVIDENCE

- Preoperative Education and Perioperative Planning
- Transitioning to outpatient care and Discharge Education
- Methods of Assessment for Pain and Respiratory Depression
- Use of Cognitive and Physical Modalities
- Use of Peripheral and Neuraxial Analgesia
- Organizational structure, policies and procedures