Multimodal Analgesia: Concepts and Strategies to Reduce Opioid Use

Jeffrey E. Janis, M.D., FACS
Professor of Plastic Surgery, Neurosurgery, Neurology, and Surgery
Chief of Plastic Surgery, University Hospital
Past President, American Society of Plastic Surgeons
The Ohio State University Wexner Medical Center

Disclosures

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Why Should We Care?

Epidemic!

- “Prescription drug overdose is an epidemic in the United States. All too often, in far too many communities, the treatment is becoming the problem”

Tom Frieden
Former Director, CDC
August 10, 2017

- White House declared that the United States was in a state of national emergency over the opioid crisis

President Donald J. Trump Directs Administration to Use All Appropriate Authority to Respond to Opioid Emergency [press release]. Washington, DC, August 20, 2017.

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How Big Is the Pain Problem?

- 80% of patients experience acute pain after surgery
- 75% of U.S. patients report surgical pain rated 7 or higher (scale of 1–10)
- 59% of patients are concerned about postoperative pain

Opioid Epidemic!

- U.S. contains 4.6% of the world’s total population, but consumes 2/3 of the world opioid supply
- 12.5 million people, or 4.7% of the American population, aberrantly used prescription opioids in 2015
- 1% of the U.S. population is addicted to opioids

North American Problem, not just U.S.!

- The issue is especially severe in the US and Canada due to pharmaceutical advertising and opioid prescription practices

Surgeon General’s Report [Internet]. Available from: https://addiction.surgeongeneral.gov/

Opioid Epidemic

- **1996-2006**: Rate of prescription opioid use disorder increased by 167%
  - Rates continued to rise
- Resurgence of heroin
  - Cheaper
  - Inappropriate weaning strategies from prescription opioids

National Data

- **1990-2010** - Prescription rate increased by 1000%
- **2015** - 28,647 people died in the U.S. due to prescription opioid overdose
- **2016** - 2,458 people died in Canada, representing an increase of approximately 200% from the previous year
- Prescription opioid use disorder is estimated to cost the American economy $53.4 billion/year

Prescribing Patterns and Deaths

- In patients with opioid prescriptions that overdose, the mortality rate increases with escalating dose.

- Unfortunately, ↑ in opioid prescription rate not resulted in improvement in patient disability or health outcome.
  - Addictive
  - Low therapeutic ratio
  - Lack of documented effectiveness in chronic pain treatment

Trends and Costs

- 4/5 heroin users report their initial exposure to opioids was to prescription opioids.

- 2007 - Prescription opioid overdose responsible for more deaths than heroin and cocaine combined.


Shocking Statistics

**DRUG OVERDOSES**

**KILL MORE THAN CARS, GUNS, AND FALLING.**

- **Falling**: 28,360 deaths
- **Guns**: 32,351 deaths
- **Traffic accidents**: 33,692 deaths
- **Drug overdoses**: 41,340 deaths

(10,297 from opioid pain medicine)


- **Accidental deaths/year in U.S.**:
  - #1 - Drug poisoning
    - 40% of drug poisonings are due to opioid overdose
  - #2 – Automobile accidents

- Exceeds deaths from HIV at the peak of the 1995 epidemic

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**US Commission on Combating Drug Addiction and the Opioid Crisis**

- “With approximately 142 Americans dying every day from the opioid crisis, America is enduring a death toll equal to September 11th every three weeks.”

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Costs

- **Estimates:** >$1 trillion from 2001 to 2017
- **Projections:** +$500 billion by end 2020


Costs

- **Sources:**
  - Lost wages
  - Lost productivity
  - Lost taxes
  - ER visits
  - EMS
  - Treatment
  - Prevention

Starting Young

- **U.S.** - 5.4% of grade 12 high school students aberrantly used prescription opioids within the last year
  - 40% stated that these drugs were easy to get
- **Canada** - 20.6% of high school seniors aberrantly used opioid medication in the last year
  - 70% of them obtaining the medications from their own homes

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Ohio Data

- In 2017, Ohio led the nation in:
  - Opioid overdose deaths
  - Heroin-related deaths
    - 1 in 9 heroin deaths in the U.S. occur in Ohio
  - Synthetic opioid-related deaths
    - 1 in 14 synthetic opioid-related deaths occur in Ohio
- Higher than CA (2nd) and NY (3rd)

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Ohio Department of Health: 2018 Ohio Drug Overdose Data

Ohio Data - Trends

- In 2018, **22.5% decrease** in deaths (vs. 2017)
- In 2018, **72.6%** of deaths involved illicit fentanyl or fentanyl analogs
- Deaths related to natural and semisynthetic opioids (e.g. oxycodone, hydrocodone) decreased by **42.0%** from 2017 to 2018

Ohio Data - Trends

- 2018 – 468M doses
- 2017 – 569M doses
- 2016 – 631M doses
- 2012 – 793M doses

- Change in 6 years: ↓ 37%!
- Decrease of 325M doses!


So Where Do These Opioids Come From?
Diversion

- Illicitly obtained prescription opioids are often obtained from friends or family.
- 40% of Medicaid patients with opioid prescriptions had indicators of aberrant use or diversion.


Surgeon’s Role

- Surgeons responsible for 9.8% of the total opioid prescriptions in the U.S.
- Rates of opioid prescriptions to opioid naïve patients after minor surgery increased between 2004-2012.

Surgeons may play a significant role in propagating the addiction crisis by exposing patients to potentially harmful and addictive opioid medications and contributing to the street supply of opioids.

Opioids and Surgery

- A 2016 study of 59,725 elective hand surgery patients showed 13% were still taking opioids 90 days after surgery.

- Another study found that 3.1% were still taking opioids at 90 days after major surgery.


### Opioids and Surgery

- **Total knee arthroplasty** - 1.4% chance of still taking opioids one year after surgery
  - Odds ratio of 5:1 when compared to non-operated controls

- Another study found that older patients (>66 y.o.) following low-risk surgery have a 44% increased likelihood of chronic use at one year compared with controls


### Leftovers and Disposal

- Elective hand surgery study (2012) - 95% received opioids with average 30 doses
  - 19 doses leftover after acute pain resolution

Leftovers and Disposal

- **Urology** - 92% received no instructions on how to dispose of leftover opioids after surgery
  - 67% had leftover opioids
  - 91% of the patients with leftovers went on to keep them in an unlocked medicine cabinet

Oral surgery and pediatric surgery – similar to above

Thoracic and gynecologic surgery - 83% had leftover opioid medication
  - 71-73% stored the leftovers unsafely

Don’t Eat the Leftovers!

- **Bicket et al.** - Systematic review to quantify unused postoperative prescription opioids
  - 67-92% of patients reported unfilled opioid prescriptions
  - Even if filled, 42-71% of all opioid tablets obtained by patients remained unused
  - <9% of patients with extra opioid tablets followed proper disposal methods

We Are Part of the Problem!

Since most people with prescription opioid use disorder get them from friends and family, it is reasonable to conclude that our postoperative analgesia prescription practices are making a significant contribution to the supply of illicit opioids.

Take Home – Surgery Is A Risk Factor

Risk of persistent opioid use following exposure to opioid medications in the perioperative period, even in opioid naïve patients.
Surgery and Addiction

- Patients who were opioid naïve before surgery shown to have a significant chance of persistent postoperative opioid use
- Many patients continue to receive opioids chronically after initially receiving them for post-operative pain control
- Patients taking opioids chronically prior to surgery have an increased chance of still taking them one year later when compared with controls


Wide Variability in Prescribing Practices

- Hill et al. - Wide variation in the number of opioid tablets prescribed
  - Even for patients undergoing the same outpatient general surgery procedure (n=642)
- Thiels et al. - Examined prescribing practices of 138 common elective procedures between 3 medical centers and reached similar conclusions (n=7,651).

Prescribing Practices Need to Change

- Opioid needs of patients could be met with much lower prescriptions
- May ↓ risk of diversion
- Post-operative opioid usage among surgeons is inconsistent
  - Benefit of more clinician opioid management training

“See One, Do One”

- Post-operative pain management teaching is lacking in many surgical residency programs
- Trainees are heavily influenced by their superiors in post-operative prescribing patterns
  - Often prescribe opioids to excessive amounts
  - Do not receive formal opioid use training

New Opioid Prescribing Laws

For first opioid prescription for acute pain:
- Adults: 7 days
- Minors: 5 days
- Cannot exceed average of 30 OMEs per day (28 oxycodone 5 mg)

Exceptions:
- Specific reason (surgery) documented in medical record
- Cancer, palliative/hospice care, addiction treatment
- Inpatient prescriptions

Surgeon’s Role

- Simple education interventions for patients to explain how to safely store and dispose of opioid medications can make a significant impact
- Led by the surgeon and a written handout or referral to a website which explains proper opioid storage and disposal

Citation: [Link to citation]


Proper Storage and Disposal

- **Opioids should be stored in a locked cabinet**
- **All un-used medication should be returned to the pharmacy or destroyed once post-operative pain has resolved**

Patient Education is Easy and it Works!

<table>
<thead>
<tr>
<th>Proportion of Parents Who Kept Child’s Leftover Pain Medication at Home</th>
</tr>
</thead>
<tbody>
<tr>
<td>Provider discussed what to do</td>
</tr>
<tr>
<td>26%</td>
</tr>
</tbody>
</table>

Patient Education is Easy and it Works!
Patient Education is Easy and it Works!


Opioid disposal rate from 11% to 22%

What Is The Clinical Impact of Ignorance of Ineffective Pain Control?
**Impact of Inadequate Pain Management**

- Undesirable **physiologic and immunologic effects**
- Associated with **poor surgical outcomes**
- ↑ probability of hospital **readmission**
- ↑ **cost of care**
- ↓ **patient satisfaction**

**Clinical Impact of Poor Pain Control**

- Uncontrolled postoperative pain:
  - Limits patient mobility
  - Decrease respiratory effort
  - Increase sympathetic discharge
- May decrease blood **flow** to healing **tissues**

Pain = Wound Healing Problems

- McGuire et al
- Post-surgical pain intensity was associated with delayed wound healing


Opioid Related Adverse Events

- Primary component of most postoperative multimodal pain management strategies
- Associated with unwanted and severe adverse events
  - Nausea and vomiting
  - Pruritus
  - Sedation and cognitive impairment
  - Urinary depression
  - Sleep disturbances
  - Respiratory depression

Getting Away from the “Cookie Cutter” Approach to Pain Management

- Common pain management protocols are opioid based
- Lack understanding of current literature
- Don’t differentiate between acute and chronic pain
- Aren’t customized to patients or surgical procedures


Effective Strategies

- Pre-op
- Intra-op
- Post-op
Pre-op

Risk Factors for Opioid Abuse

- History of substance use disorder
- Co-morbid psychological health conditions (i.e. anxiety, depression)
- Male sex
- Low socioeconomic status

Risk Factors for Chronic Opioid Use Following Surgery

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Odds Ratio</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Demographics</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>1.56</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Age &gt; 65 years</td>
<td>1.74</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>History of drug use</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Benzodiazepines</td>
<td>1.02</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Anti-anxiety Medication</td>
<td>1.05</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Anti-psychotics</td>
<td>1.14</td>
<td>0.18</td>
</tr>
<tr>
<td>Mental Concomitants</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Depression</td>
<td>1.19</td>
<td>0.09</td>
</tr>
<tr>
<td>Psychosis</td>
<td>1.01</td>
<td>0.08</td>
</tr>
<tr>
<td>Alcoholic Abuse</td>
<td>1.03</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Drug Abuse</td>
<td>0.15</td>
<td>&lt; 0.001</td>
</tr>
</tbody>
</table>

Risk Factors for Opioid Abuse

- Patients presenting for surgery with a chronic pain condition and on an opioid medication have greater morbidity and mortality, as well as increased health care costs following orthopedic and abdominal surgeries compared with controls.

| Preoperative Opioid Misuse is Associated With Increased Morbidity After Elective Orthopedic Surgery |
|---------------------------------|----------------|----------------|
| 90-Day Costs                    | $24,263        | $36,604        |
| Length of Stay                  | 5.2 days       | 5.9 days       |
| Major Complications             | 16%            | 20%            |
| Non-Home Discharge              | 11%            | 13%            |
| Hospital Readmission            | 6%             | 10%            |


Chronic Opioids

- It has been suggested that 5-25% of patients on a chronic opioid medication have an opioid use disorder.

Additional clinical features of opioid dependence

- Taking a high dose or a rapidly escalating dose despite stable pain condition
- Past or strong family history of addiction
- Only one type of opioid works
- Deteriorating or poor social functioning
- Binging on opioids
- Reporting opioid withdrawal symptoms
- Acknowledging being addicted
- Currently addicted to other drugs (coca, benzodiazepines, cannabis, etc.)
- Underlying mood or anxiety disorders not responsive to treatment
- Inconsistent urine drug screen results
- Concern expressed by family members

Recommendations

- Patients with an established or suspected substance use disorder should be referred to an addiction specialist pre-operatively if possible.
- Elective surgery in patients with established substance use disorders should not be performed until follow-up for substance use has been arranged.

<table>
<thead>
<tr>
<th>Risk Factors for Adverse Outcomes of Opioid Therapy and Opioid Misuse</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
</tr>
<tr>
<td>Opioid dose &gt;50 morphine equivalent (mg/day)</td>
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<tr>
<td>Sedative hypnotic use</td>
</tr>
<tr>
<td>Alcohol or drug use history</td>
</tr>
<tr>
<td>Depression or other mental health disorder</td>
</tr>
<tr>
<td>Past incarceration or legal problems</td>
</tr>
<tr>
<td>Smoking</td>
</tr>
<tr>
<td>Higher reported pain severity</td>
</tr>
<tr>
<td>Younger age</td>
</tr>
<tr>
<td>Family history of substance abuse</td>
</tr>
</tbody>
</table>

What is the Role of Intra-Op Narcotics?

Opioid Hyperalgesia

- Common misconception that tolerance to opioids is a slow process
- Opioid tolerance starts to develop within a matter of minutes
- So, patients who receive higher doses of narcotics intraoperatively require more narcotics postoperatively

Opioid Hyperalgesia

Common Characteristics of Opioid-Induced Hyperalgesia
- Worsening pain over time in spite of and because of increases in opioid dose
- Nociceptive sensation
- Area of pain more diffuse
- Pain of lesser quality and harder to pinpoint

Opponent Process Theory

Other Intraop Strategies
Surgical Site Infiltration: Best Clinical Practice

- **Solution**
  - Bupivacaine (150 mg) or Ropivacaine (300 mg)
  - Additives to prolong duration (e.g., clonidine 100 mcg, epinephrine 0.5 mg)
  - Liposomal bupivacaine

- **Volume**
  - 40-100 mL

- **Use a 22 gauge, 1.5-inch needle**
- **Use a fanning technique** (“moving needle technique”)
- **Needle is inserted approximately 0.5-1 cm into the tissue plane and local anesthetic solution is injected while slowly withdrawing the needle (reduces the risk of intravascular injection)***

Liposomal Bupivacaine

Solution

- Liposomal bupivacaine 266mL 20mL
- 0.25% bupivacaine 30mL
- Sodium Chloride 0.9% 100mL
- Total volume 150mL
Liposomal Bupivacaine in Abdominal Wall Reconstruction

Cost Effective in Plastic Surgery?

- Queried Vizient Database on plastic surgery procedures
  - Cosmetic and recon
- Looked at LOS, readmission rates, direct and total costs

Cost Effective?

- 958 cases
  - Liposomal bupivacaine used in 25% (239 cases)
- ↓ LOS (5.8 vs. 9.2 days)
- ↓ Cost
  - Total: $28K vs. $39K
  - Direct: $18K vs. $24K
- Similar readmission rates


Post-Op Strategies
ERAS Background

- Initiated by Dr. Kehlet in the 1990s
- Also referred to as ‘fast-track’ surgery
- Official protocols exist for:
  - GI Surgeries
  - Radical cystectomy for bladder CA
  - Head and Neck Cancer
  - Gynecologic Oncology
  - Breast Reconstruction
  - Bariatric Surgery
  - Abdominal Wall Reconstruction

- Embraced in American, European and Canadian Institutions
- Shown to:
  - Reduce length of stay
  - Decrease postoperative complications
Six Core Principles of ERAS

1. Patient and family engagement
2. Nutrition management
3. Perioperative fluid and hydration management
4. Perioperative early mobility and physical activity
5. Surgical best practices
6. Multi-modal opioid sparing analgesia

Multimodal Analgesia
The Basics
Multiple Organizations Have Urged a Shift Toward Non-Opioid Options for Pain Management

- **JCAHO:**
  - “An individualized, multimodal treatment plan should be used to manage pain—upon assessment, the best approach may be to start with a non-narcotic”

- **CDC:**
  - “Health care providers should only use opioids in carefully screened and monitored patients when non-opioid treatments are insufficient to manage pain”

- **ASA:**
  - “A multimodal approach to pain management beginning with a local anesthetic where appropriate”

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How Can we Best Reduce Surgical Pain?

- Use **clinically relevant outcome measures** instead of pain score scales
- Avoid and/or limit opioid use
- Use **multimodal anesthesia** regimens
- Develop clinical pathways using a **procedure-specific approach**
  - PROSPECT Guidelines
- Avoid analgesic gaps

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Analgesic Options For Multimodal Analgesia

- Regional analgesic techniques
  - Wound infiltration
  - Field blocks (TAP block)
  - Peripheral nerve and plexus blocks
  - Neuraxial blocks
- IV Lidocaine infusion
- Acetaminophen
- NSAIDs
- COX-2 inhibitors

- Dexamethasone
- Ketamine
- Gabapentin/pregabalin
- Opioids (as rescue)

Multimodal Pain Management

- Combines a variety of analgesic medication and techniques with nonpharmacological interventions
  - Uses drugs with complimentary mechanisms of action
  - Targets multiple sites of the nociceptive pathway
- Allows for lower doses of medications and potentially provides greater pain relief
- May result in fewer analgesic side effects
- May address patient differences in analgesic metabolism and pain sensitivity

Benefits of Multimodal

- Improve postsurgical pain control
- Permit use of lower analgesic doses
- Reduce dependence on opioids for postsurgical pain management

Golembiewski J and Dasta J. Clin Ther. 2015. [Epub ahead of print]

Multimodal Regimen

- PRIOR TO SURGERY
  - 300 mg Gabapentin (Neurontin) by mouth
  - Only if no history of sleep apnea
Multimodal Regimen

- **Upon arrival to the surgery center or hospital**
  - 1500 mg acetaminophen by mouth liquid (2 hours prior to surgery time)
    - If no hypersensitivity, severe hepatic impairment or severe active liver disease
  - 300 mg Gabapentin by mouth (2 hours prior to surgery time)
    - Only if no history of sleep apnea
  - **400 mg celecoxib** by mouth (20 minutes prior to surgery time)
    - Depends on assessment of individual patients risks (cardiovascular morbidity, gastroduodenal ulcer history, renal function and hepatic function)
  - 40 mg aprepitant (Emend), 1 tablet by mouth, 2 hours before surgery*
    - *(Only if history of post op nausea and vomiting AND ONLY before operation, never post operation)*

Sample Multimodal Regimen

- **Intraoperative**
  - **Multi-planar field block** with 0.25% Marcaine with epinephrine or liposomal bupivacaine
  - **Ketorolac IV** (15-30 mg)
    - Don’t currently have IV acetaminophen or IV ibuprofen
  - **Dexamethasone IV** (8 mg)
    - Improves pain control, reduces PONV, anti-inflammatory
    - No significant effect on blood glucose
Timing of Perioperative Analgesia

- Timing of the block (pre- vs post-incision) does **not** appear to be clinically significant
- Nerve blocks improve postop analgesia
- Total dose, but not volume and concentration, of LA affects the efficiency


Sample Regimen

- **Day of Surgery/POD#0**
  - **200 mg celecoxib** by mouth (12 hours after the morning dose)
  - **1000 mg acetaminophen** tablet by mouth (every 6 hours, repeat 3 times)
  - **5 mg oxycodone** 1 tablet by mouth every 4 hours as needed for pain
  - **100 mg docusate (Colace)** 1 tablet by mouth 2 times a day as needed for constipation
  - **8 mg odansteron** sublingual 1 dissolvable tablet every 8 hours as needed for nausea
Sample Regimen

- **POD#1 and after**
  - **200 mg celecoxib** by mouth, 3 times a day for 10 days
  - **1000 mg acetaminophen** tablet by mouth every 6 hours for 6 days *(with no other APAP-containing meds!)*
  - **5 mg oxycodone** 1 tablet by mouth every 4 hours as needed for pain
  - **100 mg docusate (Colace)** 1 tablet by mouth 2 times a day as needed for constipation for 4 days
  - **8 mg odansteron** sublingual 1 dissolvable tablet every 8 hours as needed for nausea

Gabapentinoids

- Beneficial when **high probability of prolonged, persistent pain**
- Reduce both pain and opioid requirements
- Can improve perioperative **sleep and anxiety**
- **< 65 y.o.:**
  - **Gabapentin 300 mg** by mouth 3 times a day for 7 days
- **> 65 y.o.:**
  - **Gabapentin 300 mg** by mouth, 2 times a day for 7 days
    - Need to adjust for renal function
Alternates

- If allergic to celecoxib or insurance won’t cover, can use meloxicam 15 mg by mouth twice a day

- If cannot take celecoxib or meloxicam, use either ibuprofen 400 mg by mouth every 6 hours or Naprosyn 440 mg by mouth every 12 hours.
  - Do not use if patient with history of peptic ulcer disease.
  - Do not take both, only one or other.

Summary
Surgeon’s Responsibility

- If an opioid naive patient develops an opioid use disorder after surgery, that is a surgical complication.

- Similarly, if members of our patients family (i.e. children, home care workers etc.) aberrantly use the medications we prescribe, we hold a level of responsibility for this.

- As surgeons we are in a unique position to lead practice change and create responsible perioperative prescribing practices.

Surgeon Suggestions

- We can make a major contribution by curbing opioid diversion in the perioperative period.

- We can partner with our anesthesia/pain colleagues to identify at risk patients and prevent postoperative aberrant opioid use.
Summary – Patient Screening

- **Substance Use Disorder** - refer to addiction specialist perioperatively

- **Risk Factors** (mood disorder, family history of substance disorder, psycho social stressors)
  - Communicate risk non-judgementally to patient and primary care physician

Summary-Prescribing Practices

- **Limit potency** of prescribed opioids
- **Limit total prescription to 20 doses** unless specific reason otherwise
- **Never prescribe long acting opioids** for acute pain
- **Use adjunctive non-opioid analgesics** (NSAIDs, acetaminophen)
Summary – Patient Education

- Risk of opioid misuse and diversion in members of household
- Proper storage of opioids in a locked cabinet
- Proper disposal practices of unused opioid medications

PRS Pain Management Supplement

Janis JE, Joshi GP.

Introduction to "current concepts in pain management in plastic surgery."