Treating Chronic Pain in a Non-Opiate-Based Format

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Disclosures

- John Dombrowski, MD, FASA, DABAM, and Gary Ozanich, PhD, have disclosed no relevant, real, or apparent personal or professional financial relationships with proprietary entities that produce healthcare goods and services.
Disclosures

- All planners/managers hereby state that they or their spouse/life partner do not have any financial relationships or relationships to products or devices with any commercial interest related to the content of this activity of any amount during the past 12 months.

- The following planners/managers have the following to disclose:
  - Kelly J. Clark, MD, MBA, FASAM, DFAPA – Consulting fees: Braeburn, Indivior
Learning Objectives

- Identify patients with chronic pain and addiction.
- Describe other modalities in treating pain outside of narcotic therapy.
- Recognize when and how to refer patients to the appropriate specialist so they get the care they deserve.
Disclosures & Objectives

- CEO Washington Pain Center
- ASA Secretary
- Medical Director Outlook, Bayside Recovery and Tranquility woods

Objectives:

- What can be done in treatment with patient with known addiction?
- What can be done to prevent addiction during surgery?
- Understanding medications used
- Once addiction is know, can we ever use opioids again for treatment?
Benefits and Risks of Opioid Analgesics

- Used for thousands of years to treat acute and chronic pain

- Remain a mainstay for treating moderate to severe pain not responsive to more conservative methods
  - 259 million prescriptions for opioids in 2012

- Chronic opioid therapy requires assessment of benefits vs. harms
  - The FDA has determined that respiratory depression is the most important serious adverse effect of opioids as it can be immediately life-threatening

There are NOT the patients we see
There are...
Perioperative Surgical Home

PSH model:
- Coordination & management.
- Reduce complications.
- Improve efficiencies & cost-effectiveness.

Physician Anesthesiologists:
- Variety of co-morbid conditions.
- Admission to discharge.
- Improve quality of care.
So why do we care?

- Perioperative surgical home

- With the changes in payment from Medicare, anesthesiologist will be more responsible for the care of the patient preoperatively, interoperability, and postoperatively. This is the essence of the perioperative surgical home.

- Anesthesiologist performing this service will show value to the hospital in which they work.
So why do we care?

- Is the operating room the first place we can intervene on someone who has an addiction?
- Once the patient is in any hospital system perhaps counseling and appropriate line acting medication management/methadone Suboxone could be started?
- SBIRT (Screening, brief intervention, referral to treatment) ETOH abuse in ED
Current hot topic in the media- “opioid free surgeries”

Explain that patients utilizing opioids prior to surgery present challenges; greater reliance on opioids in the post-op period, etc.

Clinical trials are needed to determine best practices for treating these patients

Explain benefits of opioid-free surgery— patients have been shown to consume less postoperative opioids leading to quicker recovery times and decreased wound infection.

Larger clinical trials need to be funded to demonstrate that combination non-opioid therapy with regional anesthesia and analgesia is superior.
Dangers of Opioid Therapy

- Hyperalgesia
- Cognitive impairment
- Tolerance
- Impaired judgment
- Addiction

- Gary M. Franklin, Opioids for chronic noncancer pain: A position paper of the American Academy of Neurology; Neurology 2014;83:1277-1284
This is why we care
Consider the Multidisciplinary Team Approach

Integrated  Coordinated  Interdisciplinary

Primary Clinician

- Pain Specialist
- Psychiatrist
- Neurologist
- Physiatrist
- Psychologist
- Occupational Therapist
- Physical Therapist
- Nurses
- Surgeon
- Pharmacist
- Social Worker
- Anesthesiologist
- Nurse Pract / Physician Asst.
How Pharmacotherapeutics Affect the Nervous System

Central sensitization
- Anticonvulsants
- Opioids
- Tricyclic/SNRI/antidepressants

Peripheral sensitization
- NSAIDs
- Topical Analgesics
- Anticonvulsants
- Tricyclic Antidepressants
- Opioids

NB. Many of these treatments are off-label
Tricyclic antidepressants

Effects  Serotonin and noradrenaline reuptake inhibitor sodium channel blocker NMDA receptor

Starting dose 10-25 at bedtime maximum dose 150 mg daily.

Adverse side effects  cardiac conduction blockage/arrhythmia, sedation, confusion, anticholinergic side effects (dry mouth, constipation, urinary retention, blurred vision) orthostatic hypotension weight gain.

Caution with elderly and especially with large prostates, chronic constipation, glaucoma, caution with concomitant use of SSRI and SNRI and tramadol.
Newer versions of the tricyclic antidepressants/SNRI

Duloxetine / Cymbalta serotonin and noradrenaline reuptake inhibitor. 
30 mg daily maximum dose 120 mg daily

Venlafaxine / Effexor serotonin and noradrenaline reuptake inhibitor 
37.5 mg once or twice daily maximum dose 225 mg daily

Side effects

mania, seizures, bleeding tendencies especially on anticoagulation therapy risk with other SSRI and tramadol

Caution with hypertensive patients cautions with use with SSRI and tramadol.

Mayo Clinic proceedings March 2010 ,85 S15-25
Serotonin are a group of G proteins and found in the central and peripheral nervous system they mediate both excitatory and inhibitory neurotransmission.

Serotonin receptors modulate release of many neurotransmitters glutamate, dopamine, epinephrine, norepinephrine, acetylcholine. Serotonin receptors also modulate hormones: oxytocin, prolactin, vasopressin, cortisol, substance p

There are seven general serotonin receptor classes and a total of 14 known serotonin receptor types.
What are Serotonin and noradrenaline receptors?

Norepinephrine hormone and neurotransmitter.

This neurotransmitter mobilizes the brain and body for action. Increased heart rate, increased blood pressure, increased glucose, increased blood flow to muscles lowers gastric mobility.
What are NMDA receptors?

N-methyl-D-aspartate receptor

Glutamate receptor these receptors are important for controlling synaptic plasticity in memory function

Activation of the receptor opening ion channel allows depolarization of the cell.

Many psychotropc/psychoactive drugs phencyclidine (PCP) alcohol, dextromethorphan (DXM) methadone and ketamine work on this receptor.
Antiseizure medications
Gabapentinoids /Neurontin Lyrica/Pregabalin

Calcium channel alpha and Delta ligand receptors reduce release of presynaptic transmitters. Similar to endogenous neurotransmitter GABA. Gabapentin modulates enzymes involved with GABA biosynthesis.

**Effect:** Has a wide variety of use outside of seizures, diabetic neuropathy, hot flashes, restless leg syndrome & anxiety.

Neurontin dosing 100-300 mg at bedtime maximum dose 3600 mg daily

Lyrica dose of a 5 mg twice daily. Maximum dose 600 mg daily.

**Side Effect:** sedation, dizziness, weight gain, blurred vision

Abuse potential is 1.1% in general population 22% in those with previous addiction—“Johnnies”

Other antiseizure medications.

Sodium channel blockers.

Carbamazipine (Tegretol) and Oxcarbazepine (Trileptal)

Effect: Work on the sodium channel decreases presynaptic transmission

Side effects: somnolence, dizziness, headache, ataxia, nystagmus, blurred vision, rash, hyponatremia, low white cell count, low platelet count, hepatotoxic

Mixing up the medicine

Anesthesiologist and physicians who specialize in pain medicine often used concomitant therapy.

However, when mixing medications when needs to be cautious of interactions of these medications.

Adverse drug reactions are major public health problem especially in the elderly 3%-6% all hospital admissions are related to this matter.

Adverse drug reactions are the fifth leading cause of death in the United States for over the past 30 years.

Drug to drug interactions relate to a pharmacokinetic (with the body does the drug) interactions. Usually at the hepatic level due to enzymes being used for processing medications. Either making the medications ineffective or over effective.

Significant drug to drug interactions

Hepatic/liver metabolism of medications CYP2D6 enzyme for metabolism. Patients can have excessive metabolizer, ultra-rapid metabolizers or for metabolizers

Nonsteroidal anti-inflammatory drugs (NSAID) affect blood coagulation. Antidepressants that inhibit serotonin reuptake also impair coagulation leading to gastrointestinal bleeding.
Serotonin syndrome

One or more serotonergic medications given. SSRIs, SNRI MAOI, TCA, amphetamines, dextromethorphan, tramadol, St. John's wort, ecstasy, cocaine, ondansetron.

Symptoms

High body temperature, agitation, hyperreflexia, tremor, sweating, dilated pupils, diarrhea. Possible seizures possible muscle breakdown

Management

Stopped the medication sedation/ benzodiazepine use, active cooling, control of blood pressure
Getting back to treating patients with SUD or potential addiction

The thought process is the same how we treat patients with the possibility of addiction, not addiction or substance use disorder.

Concomitant therapy: medication management, psychologic expectations, injection techniques, surgical techniques, continuation medications postoperatively.
Effects of Opioid vs Nonopioid Medications on Osteoarthritis Pain-Related Function

Erin E. Krebs, MD, MPH; Amy Gravely, MA; Sean Nugent, BA; et al

Original Investigation | March 6, 2018
Treatment options

- Bandages, heat and or cold application.
- Mechanical device (splint), physical and occupational rehabilitation
- Biofeedback, cognitive behavioral therapy, distraction, desensitization, goal setting and pace strategy, guided imagery, hypnosis, psychotherapy for depression and anxiety, relaxation techniques.
- Interventional
  - Injections/external beam radiation/spinal cord stimulation surgery
Pre Operative treatment

- Ask questions
- Previous issue with post op pain
- Plan intra and post operative treatment
- Set *reasonable* expectations
- Consider providing these patients with pre meds days prior to surgery
Persistent pain in postmastectomy patients: Comparison of psychophysical, medical, surgical, and psychosocial characteristics between patients with and without pain

Kristin L. Schreiber\textsuperscript{a,b,*}, Marc O. Martel\textsuperscript{b}, Helen Shnol\textsuperscript{a}, John R. Shaffer\textsuperscript{c}, Carol Greco\textsuperscript{d}, Nicole Viray\textsuperscript{a}, Lauren N. Taylor\textsuperscript{a}, Meghan McLaughlin\textsuperscript{a}, Adam Brufsky\textsuperscript{e}, Gretchen Ahrendt\textsuperscript{f}, Dana Bovbjerg\textsuperscript{e}, Robert R. Edwards\textsuperscript{b,g}, Inna Belfer\textsuperscript{a,c}

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\textbf{200 patients were studied & followed for 4 years}

<table>
<thead>
<tr>
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<th>No PPMP group n = 98</th>
<th>PPMP group n = 102</th>
<th>P value</th>
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<tbody>
<tr>
<td>Age</td>
<td>59.3 (10.2)</td>
<td>58.3 (10.5)</td>
<td>0.685</td>
</tr>
<tr>
<td>Body mass index</td>
<td>28.3 (5.7)</td>
<td>29.0 (5.8)</td>
<td>0.46</td>
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<tr>
<td>Anxiety</td>
<td>12.5 (5.2)</td>
<td>14.4 (6.4)</td>
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<tr>
<td>Depression</td>
<td>10.6 (4.1)</td>
<td>12.2 (6.1)</td>
<td>0.003</td>
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<tr>
<td>Catastrophizing</td>
<td>2.1 (4.0)</td>
<td>7.2 (8.9)</td>
<td>0.000</td>
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<tr>
<td>Situational catastrophizing</td>
<td>1.18 (1.96)</td>
<td>1.12 (2.05)</td>
<td>0.692</td>
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<tr>
<td>Somatization</td>
<td>8.3 (2.8)</td>
<td>10.4 (4.1)</td>
<td>0.003</td>
</tr>
<tr>
<td>Perceived stress</td>
<td>15.1 (5.9)</td>
<td>16.5 (6.1)</td>
<td>0.104</td>
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<tr>
<td>Sleep disturbance</td>
<td>20.0 (8.1)</td>
<td>24.2 (8.9)</td>
<td>0.01</td>
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\textbf{Conclusion:} The patients psychophysical & psychosocial profile was predictor of chronic pain
Acute Postoperative Pain

- Severity of acute postoperative pain is a strong predictor for development of *Persistent Postoperative Pain* (PPP) at 3 months

- The duration (1-7 days) of severe postoperative pain is also a strong predictor of PPP
Surgery and Acute Pain Mediators

Humeral mediators

Regional Analgesia: Neuronal conduction

Surgery

Spinal Cord
Multimodal Analgesia

- **Definition**: Multimodal analgesia is the combination of different analgesics that act by different mechanism, resulting in additive or synergistic analgesia with lowered adverse effects; compared to sole administration of an individual pharmacological agent.

- **Goal**: Decrease use of Postoperative Opioids
Multimodal Analgesics for Postoperative Pain

Ketamine, Dextromethorphan, Memantine, Gabapentin, Pregabalin, COX-2 inhibitors, Acetaminophen

Ketamine, Dextromethorphan, Magnesium, Clonidine, Dexmedetomidine, Gabapentin, Pregabalin, Neostigmine, Local anesthetics, COX-1 and COX-2 inhibitors, Tapentadol

Clonidine, Steroids, Neostigmine, local anesthetics
Meta-analyses: NSAIDs, COX-2 inhibitors & Acetaminophen

- 52 RCT were included:

Results:
- 24 h morphine consumption: ↓ 20 - 40 %
- Postoperative VAS: ↓ 10-15 %
- Opioid related AE: ↓ 15 – 25 %

Adverse events:
- Severe bleeding: 0 to 1.7%
- Renal insufficiency in cardiac patients: 0 % to 1.4%

Alpha – 2 Agonist
Effect of systemic alpha 2 agonist on postoperative pain intensity

- 13 RCT with clonidine and dexmedetomididine (n=1792 patients)

<table>
<thead>
<tr>
<th></th>
<th>↓ Morphine consumption</th>
<th>↓ Pain Scores</th>
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<tbody>
<tr>
<td>Clonidine</td>
<td>4.1 mg</td>
<td>0.7</td>
</tr>
<tr>
<td>Dexmedetomidine</td>
<td>14.5 mg</td>
<td>0.6</td>
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- Side effects: Hypotension and bradycardia
NMDA Antagonist
Ketamine as a Multimodal Agent

- In RCT, perioperative ketamine use:
  - Has led to opioid dose ↓ by 30%
  - ↓ of chronic post-surgical pain syndromes

- Dose:
  - 0.1 - 0.5 mg/ kg bolus ± 0.1- 0.5 mg/kg/hr infusion

- Side effects:
  - < 10% of patients had complains of psycho-cognitive effects.

Visser E et al: *Biomedicine & Pharmacology* 2006; 60: 341
Gabapentin for Perioperative Pain Control: Meta-Analysis

- **18 RCT of 1181 patients**
- **Dose of gabapentin: 1200 mg daily**
- **Outcome:**
  - ↓ Pain scores at 24 hours by 27%
  - ↓ 24 hour opioid use by 35%
  - ↑ Sedation in the postoperative period
  - No difference in serous adverse events

- Similar results in a review of gabapentinoids in 2007 by Elina Tiippana et al from Finland published in *Anesth & Analg*

  **The Analgesic Effects of Perioperative Gabapentin on Postoperative Pain: A Meta-Analysis**

  Robert W. Hurley, M.D., Ph.D., Steven P. Cohen, M.D., Kayode A. Williams, M.D., Andrew J. Rowlingson, B.A., and Christopher L. Wu, M.D.
Allodynia or Hyperalgesia of Knee

Buvanendran et al: Anesth Analg 2010
Administration of local Anesthetics, Adjuvant to surgical site
Injection Techniques for acute pain management
Injection Techniques for acute pain management
How to treat your patient with SUD with Pain?
Lumbar anatomy... causes for my pain
anatomy
Definition of Neuromodulation

“Neuromodulation is the electrical or chemical modulation of the central nervous system to significantly reduce chronic pain or improve neurologic function.”
Neuromodulation

- Treatment for post lumbar/cervical laminectomy syndrome
- Pelvic and visceral pain
- Peripheral vascular disease
- Refractory angina
- Migraine-Posterior occipital syndrome
- Patient with degenerative joint disease or lumbar canal stenosis who do not wish surgery
- Neuropathy-Diabetic and Chemotherapy Studies ongoing.
Precise delivery of small doses of electricity or drugs directly to targeted nerve sites.
Neuromodulation
Neuromodulation
Neuromodulation

- The follow up...
Thanks!

ANY QUESTIONS?

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Clinical Track

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THANK YOU

#RxSummit
www.NationalRxDrugAbuseSummit.org