Opioids for Chronic Pain?

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How many?

Did you know?

1 : 3
Acute Chronic Pain

Chronic Pain

Deaths

- Quadrupling of deaths in last 15 years
- Failed efforts to consider addictiveness, low therapeutic ratio, lack of effectiveness


• Quadrupling of deaths in last 15 years
• Failed efforts to consider addictiveness, low therapeutic ratio, lack of effectiveness
New Evidence on Opioid Epidemic

- At least 60% of the overdose epidemic caused by illicit drugs, not prescription opioids.
- The increase in opioid-related deaths primarily due to illicit fentanyl use.
  - Illicitly manufactured fentanyl cannot be distinguished from prescription fentanyl in death certificate data.
- Prescription Opioid Crisis = Polypharmacy Crisis?
  - More than 50% of deaths with opioid positive toxicology included alcohol.
  - Average # of drugs identified in toxicologies = 6.
- There has been a 20% decrease in opioid prescriptions between 2013-2017.

Death Certificates

- Death Certificate Data do not distinguish:
  - Drugs pharmaceutically manufactured.
  - Prescribed by health care provider.
  - Pharmaceutically manufactured but diverted (not prescribed to the person).
  - Illicitly manufactured.

[References]


Opioid Crackdown

Vicki

“After 20 years of being on opioids during which I worked full time, raised three successful children, and took care of my house, I’m now on my last month of pain medications. I’m not sure what I’m going to do now that I can’t do much of anything. I have no hope for the future, and don’t care if I live or die anymore. This is no kind of existence.”

Toll on Pain Care

Drug Enforcement Policies
- Involuntary Tapers
- Patient Abandonment
- Practitioner Flight
- Fear of state or federal government sanctions

CDC Guideline
- Arbitrary adoption by regulators and health care organizations
  - Opioid reduction without expanding other resources for pain care
  - Leading more people to illicit opioid markets with greater harm?

Unintended Consequences of CDC Guideline

- Suicide/ideation from forced opioid cessation or reduction (Fox News, 2018)
- Human Rights Watch launching investigation
- Some feel people being tortured (Thomas Kline, MD (2018))
- Medicare limiting opioid prescriptions to 90 MME/day, and 7 days if opioid naïve (Pain Medicine News, 2018)
- CVS pharmacy limiting prescriptions to 7 days if opioid naïve, ER before ER opioids, limits to daily dose (CNN News, 2018)

Violating the “human right” to pain management?

- Many international bodies embrace idea of human right of access to pain management
- Limiting access to opioids denies a “right to access”
- U.N. Human Rights Officials
  - Failure to ensure access to controlled medicines for pain relief & suffering protection of persons from cruel, inhuman, and degrading treatment
- Solution: ensure that WHO’s Essential Medication List available and accessible to all who need them, including CNCP
- Opioids, NSAIDS, Muscle relaxants, antidepressants

BUT:
- Does not mean opioids on demand. “This is my right”
- Does mean Clinician determines best treatment option without government interference


Sickle Cell Disease

The major types of SCD-associated chronic pain include the following:

- Chronic pain often of unclear etiology: This type of chronic sickle cell pain may be an extension of recurrent acute painful episodes. Therefore, early and aggressive intervention in treating acute sickle cell pain may reduce the development of chronic pain.
- Chronic pain due to a specific tissue or organ, such as avascular necrosis (AVN) of the hips, or leg ulcers.
- Chronic pain due to nerve damage, muscle pain, and arthritis: Musculoskeletal pain may occur in the chest, back, abdomen, extremities, neck, or head and is difficult to treat.
- Chronic neuropathic pain: This is usually described as burning, numbness, tingling, shooting, or pricking in nature and is associated with a nuisance of pain and weakness. Its severity is also enhanced by exercise or other physical stress.
- Chronic pain can be secondary to either peripheral or spinal nerve injury or nerve dysfunction. SCD-related neuropathic pain has two etiologies: The first is tissue damage secondary to ischemia of bones, vessels, nerves, skin, muscles, and bone and non-cancer pain management seems to lead to neuropathic pain.

- “Breakthrough” pain is another type of pain often identified by health-care professionals who treat patients with SCD. This term literally means the act of breaking through pain called. Originally used to describe patients who cancer pain—were maintained on a stable dose of opioids. Breakthrough pain was defined as a brief episode of sudden pain in response to usual therapy. Such a break-through is usually short-lived and not chronic, and reduces pain to zero or near zero. There are currently no data that clearly describe this type of pain.

By age 35 years, half of all persons with sickle cell anemia have evidence of hip and shoulder osteo-necrosis on magnetic resonance imaging (MRI).
In conclusion, in order to help patients with SCD, they should be respected, listened to, believed, and treated with the best means available. Currently, the use of OPRs is one of the most commonly used methods. An adversarial relationship never leads to or creates a permanent solution. The current national opioid phobia may, unwittingly, deny opioids to patients who really need them, especially those patients who experience recurrent episodes of acute pain such as patients with SCD.

Nonselective NSAIDs and COX-2 selective inhibitors may be considered rarely, and with extreme caution, in highly selected individuals (high quality of evidence, strong rec)

- All patients taking nonselective NSAIDs and COX-2 selective inhibitors should be routinely assessed for gastrointestinal and renal toxicity, hypertension, heart failure, and other drug-drug and drug-disease interactions (weak quality of evidence, strong recommendation).

All patients with moderate to severe pain, pain-related functional impairment, or diminished quality of life due to pain should be considered for opioid therapy (low quality of evidence, strong recommendation)

- Patients taking opioid analgesics should be reassessed for ongoing attainment of therapeutic goals, adverse effects, and safe and responsible medication use (moderate quality of evidence, strong recommendation)

“Opioids may be considered for patients with moderate to severe pain, particularly if the pain is causing functional impairment or is reducing their quality of life.”
Safer Pharmacologic Option

- Consider adverse effects of NSAIDs
  - Nephrotoxicity, bleeding, cardiotoxicity

- Consider life-threatening drug resistance from combining antiretrovirals (ART) with certain anticonvulsants or antidepressants
  - Reduced blood levels of the ART

Opioid Evidence Base

CDC Guideline

CDC Guideline viewed only RCTs ≥52 weeks as adequate
Problem: no other analgesics held to that standard

In fact: several 52 week open label studies of ER/LA opioids show benefit and safety


Opioid Evidence Base

<table>
<thead>
<tr>
<th>Misconception</th>
<th>Reality</th>
</tr>
</thead>
<tbody>
<tr>
<td>No RCT &gt; 12 weeks</td>
<td>FDA does not require studies &gt; 12 weeks due to high placebo dropout rate</td>
</tr>
<tr>
<td>No long term studies showing pain relief beyond 12 weeks</td>
<td>Cochrane review shows over 20% of pts with chronic pain have long term relief from different painful conditions</td>
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<tr>
<td>High % of pts prescribed opioids die of overdose</td>
<td>Opioid-related deaths for prescribed opioids is 0.02%</td>
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<tr>
<td>Prescription OUD mainly due to ER opioids</td>
<td>IR opioids preferred by most with OUD</td>
</tr>
<tr>
<td>Prescription opioid abuse continuing to rise in the U.S.</td>
<td>3-4 years of steady declines</td>
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Opioids and Addiction

Misconception: Over 20% of patients on chronic opioid therapy meet DSM 5 criteria for opioid use disorder (Addiction)

Evidence: Adams et al- 12 month study of abuse with hydrocodone, tramadol, NSAIDS

Reality: abuse rates 4.9% hydrocodone, 2.7% tramadol, 2.5% NSAIDS

Opioids and Addiction

Assumption: Opioids leading chronic pain patients to addiction and overdose deaths

Evidence: “Addiction occurs in a small percentage of people exposed to opioids – even with pre-existing vulnerabilities” – Nora Volkow, Director of NIDA
Fishbain et al – 3.27% risk of addiction in review of 67 studies
Cochrane Review - 0.5% incidence of de novo addiction & prevalence 4.5%

Reality: Opioids for chronic pain not associated with a major risk of addiction (OUD)

Opioids and Addiction

Assumption: Prescription opioids first drugs abused and addiction develops quickly

Evidence: National Survey on Drug Use and Health (N=115,171)
77% used another drug (e.g., cannabis, inhalants, stimulants) before first nonmedical use of prescription opioid
65% using prescription opioids nonmedically were not prescribed the opioid
Takes 5 years from first use to non-medical use of opioid

Reality: Most with addiction do not start with a prescription from a prescriber treating a medical condition

Opioid Evidence-Base

Opioids for chronic noncancer pain: a meta-analysis of effectiveness and side effects

CMAJ 2006;174(11)
Andrea D. Farlow, Juan A. Sandveri, Angela Maisy-Gagnon, Eldon Tunks
Chronic non-cancer pain is a major health problem, for which opioids provide one Rx option. However, evidence is needed about side effects, efficacy, and risk of misuse or addiction.

Furlan A et al CMAJ 2006;174(11):1589-1594

Opioid Evidence Base
Meta-analysis 41 Trials (n = 6,019)

- Nociceptive (OA, RA, LBP): 80%
- Neuropathic (PHN, DPN, phantom): 12%
- Fibromyalgia: 7%
- Mixed: 1%
- Study quality high: 87%

Furlan A et al CMAJ 2006;174(11):1589-1594

Opioid Evidence Base
Meds Studied

- Tramadol
- Codeine
- Propoxyphene
- Morphine
- Oxycodone

Furlan A et al CMAJ 2006;174(11):1589-1594
Opioid Evidence Base

Efficacy Outcomes: Pain & Function

“Opioids were more effective than placebo for both pain and functional outcomes in patients with nociceptive or neuropathic pain or fibromyalgia.”

Furlan A et al. CMAJ 2006;174(11):1589-1594

Opioid Evidence Base

Safety Outcomes: AE’s

“Dropout rates averaged 33% in the opioid groups and 38% in the placebo groups.”

Furlan A et al. CMAJ 2006;174(11):1589-1594

Opioid Evidence Base

Efficacy Outcomes: Pain & Function

Limitations

• No clinical data beyond 16 weeks
Opioid Evidence Base
Opioids vs TCA in PHN

- 44 pts completed 3 treatment periods (opioid, TCA, placebo) for 8 wks/period
- Outcome measures: pain intensity, pain relief, cognitive function
- Opioids: controlled release morphine; methadone as alternative
- TCA: nortriptyline; desipramine as alternative
- Placebo: starch

Findings: opioids and TCA decreased pain more than placebo (p<0.001) and no detrimental cognitive effects
- Opioids and TCA produced greater pain relief (38% and 32%) vs placebo (11%)
- Trend toward greater pain reduction and lower NNT with opioids vs TCA
- Sustained release morphine compared to nortriptyline more effective in decreasing PHN pain when two drugs compared
- Pts preferred opioid to TCA (54% opioid; 30% TCA; 16% placebo)
- Comparison of TCA and opioid suggested opioids probably decrease PHN pain better than TCA
Since 2010, the quantity of prescribed opioids has consistently decreased while opioid overdose deaths have increased. Illicit opioid use is likely to increase by 61% between 2015-2025.

Prescription Drug Monitoring Programs and maximum dose regulations are predicted to decrease overdose deaths by only 3.0-3.5%.

**Opioid Epidemic Interventions**

**Opioid Therapy Safe Use**
- Patients prescribed opioids for pain likely at low risk for Addiction (OUD)
  - Monitor for problematic use, use PDMP, UDT, risk assessment questionnaire
- Counsel on storage and disposal
- Start low and gradually increase dose
- Very cautious about co-use of opioids with benzodiazepines
  - Overdose risk increased even at low doses
- Naloxone for patients at risk
- Buprenorphine or methadone for OUD
Abuse-Deterrent Opioids: Effectiveness and Value.

Economic modeling – ADF opioids have potential to substantially reduce incidence of abuse in chronic pain patients.
But – Significantly higher cost.
Call for: further research generating real-world evidence for health and economic impact on opioid abuse epidemic.

Ethical Opioid Use
- Provide opioids for cancer pain and at the end of life.
- Consider opioids for certain patients with chronic, non-cancer pain.
  - Severe pain, unresponsive to other therapies, adversely affects quality of life or function.
  - Other therapies: non-opioid meds, injections/nerve blocks, electrostimulation, PT, psychological support, integrative therapies.
- Separate overdoses from prescribed vs. illegal drugs.
- Data show increased OD deaths tied to illegal drugs.
- Preserve access for patients who function and quality of life are improved.
- Don’t drive patients to more dangerous street drugs by limiting prescribed opioids.