Prescribing Opioids in the 21st Century: It was the best of times, it was the worst of times.

ROBERT HAUPTMAN MD
PAIN CONSULTANT BODY RESTORATION
ASSISTANT CLINICAL PROFESSOR U OF A

Faculty / Presenter Disclosure

- Faculty: Robert Hauptman MD
  - Pain Consultant Body Restoration
  - Assistant Clinical Professor U of A
- Relationships with commercial interests:
  - Grants / research support: None
  - Speakers bureau / honoraria: AZ, GSK, Bi, Pfizer, Merck, Abbott, Valeant, Paladin, Bayer, Purdue and Knight
  - Consulting fees: AZ, GSK, Bi, Purdue
  - Other: Past President AMA Section of Chronic Pain and Pain Society of Alberta
Learning Objectives

- To review the opioid crisis
- To discuss the current Canadian Guidelines regarding opioid prescribing
- To discuss initiation of opioid therapy
- To discuss tapering of opioids
- To review benzodiazepines
- To briefly discuss interventional therapies

Case 1

GS
- 78 year old female patient
- Psoriatic arthritis, OA and chronic back pain
- On Hydromorph Contin 30 mg tid and dilaudid 8 mg PRN
- Average pain 8/10.
- Poor function. Not going out of home because of pain
- Not sleeping at night. Not able to do ADLs
- Pain all over.
Case 2

- RL
- 57 year old male
- Chronic mechanical back pain
- On OxyNeo 40 mg twice a day and Oxycodone 10 mg PRN
- Working full time
- Exercises
- Takes care of his elderly mother
- Average pain 3/10

Where We Are Today

- Chronic pain should be managed with a broad approach that includes pharmacological and non-pharmacological therapies
- The only intervention that works in nearly 100 percent of pain patients is exercise
- Opioids are one invaluable tool in the fight against pain – however they do not work in everyone and like all treatments have a risk benefits ratio
- Both the CDC and the Canadian Opioid Guidelines recommend opioids for some patients with chronic pain. This approach is supported by the CPSA
- The relationship between prescribing opioids to chronic pain patients and the opioid crisis is complex and not as straight forward as many are led to believe
Issues and Concerns

1 in 5 Canadians suffer from moderate/severe chronic pain

1 in 3 cancer survivors have chronic pain after curative treatment

~1% of Canadians using opioid pain relievers report using them to get high

~12% of Ontario students report using a prescription opioid nonmedically in the past year

Universality of access to pain management without discrimination


Was there a Prescription Opioid Crisis?
Statistics:

“If you torture the numbers long enough, they will tell you anything”

Anonymous
Acetaminophen overdose is a leading cause of acute liver failure in Canada.\(^1\)

NSAIDs are responsible for more than 100,000 hospitalizations and more than 16,000 deaths in the United States each year.\(^2\)

---

"Tylenol Is By Far The Most Dangerous Drug Ever Made"

Analysis of national databases show that acetaminophen-associated overdoses account for about 50,000 emergency room visits and 25,000 hospitalizations yearly. Acetaminophen is the nation's leading cause of acute liver failure, according to data from an ongoing study funded by the National Institutes for Health. Analysis of national mortality files shows about 450 deaths occur each year from acetaminophen-associated overdoses; 100 of these are unintentional.\(^3\)

Aric Hausknecht, M.D. July 30, 2017

Neurologist and Pain Management Specialist New York
National Overdose Deaths
Number of Deaths from Benzodiazepines

Source: National Center for Health Statistics, CDC Wonder

Overdose Deaths Involving Opioids, by Type of Opioid, United States, 2000-2015

NSDUH – Past Year Non Medical Use/ Opioid Use Disorder 2002-2014 (> 12 y.o.)
Introduction

Transparency, freedom from bias, and accountability are, in principle, hallmarks of taxpayer-funded institutions. Unfortunately, it seems that at least one institution, the Centers for Disease Control and Prevention (CDC), continues to struggle with all three. What began as a prescribing guideline created in secrecy has now evolved to the use of statistical data and public statements that fail to capture not only the complexity of the problem but also the distinctions between licit and illicit opioids and their relationship to the alarming increase in unintentional overdose. This is unfortunately consistent with Mark Twain’s assertion that “There are lies, there are damn lies, and then there are statistics.”

For instance, when the CDC was in the process of drafting guidelines for the use of long-term prescription opioids to treat chronic pain, the identities of the project’s Core Expert Group members remained a secret until they were leaked.1,2 When its members were eventually identified, many were concerned that the group’s composition was not balanced and had an inherent bias against the use of prescription opioids in treatment.3 Then, when the time came for public input on the draft of the prescribing guideline, the CDC’s invitation for meaningful comment was best described as a charade and a comedy of errors. For example, the only way the public could view the draft was during a one-time internet webinar. The actual guideline itself was not publicly available and was not posted on the CDC website, and admission to the webinar was limited. Those fortunate enough to gain entry were sometimes able to see the actual recommendation as it flashed on the screen, and while attendees were permitted to ask questions, the CDC stated that they would not provide any answers. By the end of the webinar, attendees could then email their comments to the CDC, but they only had 25 hours to do so. This was followed by an endless parade of critical feedback and sometimes angry responses. Eventually, the CDC decided to repeal the rule on the following day and allow an additional 24-hour comment period.6 The controversy did not end there. Following the webinar on the following day and allow an additional 24-hour comment period.4 But the webinar on the following day and allow an additional 24-hour comment period.4 But the comment can be best described as somewhere between a charade and a comedy of errors. For instance, when the CDC was in the process of drafting guidelines for the use of long-term prescription opioids to treat chronic pain, the identities of the project’s Core Expert Group members remained a secret until they were leaked.2,3 When its members were eventually identified, many were concerned that the group’s composition was not balanced and had an inherent bias against the use of prescription opioids in treatment.4

There is not an opioid crisis but a polypharmacy crisis

Aound number of drugs in people who have died from opioid deaths were six

Prescription opioids dispensed in the US from 2010 to 2015 has dropped by over 18%

Surveys have indicated that 50% of US physicians have cut back their opioid prescribing – 10% have stopped prescribing opioids

Opioid deaths continue to climb
“…..we need to make good use of what we know about the role that prescription opioids plays in the larger crisis: that the dominant narrative about pain treatment being a major pathway to addiction is wrong, and that an agenda heavily weighted toward pill control is not enough”

Dr. Sally Satel Psychiatrist and Addiction Physician
Yale University School of Medicine
February 2018

In this study of over 2,000,000 prescriptions of opioids for chronic pain, overall death rates from opioids was 7 deaths per 10,00 person years. This rate increased by 7 fold if BDZs were added.

Opioid Crisis?

- Any death from an opioid is unfortunate
- HOWEVER deaths from opioids prescribed for legitimate medical reasons and used as intended is small
- A crisis of chronic pain confounded by a crisis of education and uniformed prescribing
- A crisis of addiction
- A crisis of illicit fentanyl deaths
2017 Opioid Guidelines Summary

1. Try other treatments before opioids
2. If tried other Txs and low risk → trial of opioids
3. Active SUD and pain – don’t use opioids
4. Active psych disorder – stabilize MH first
5. Hx of SUD, tried non-opioids – don’t use opioids
6. Starting new patient – limit to 50mg ME
7. Starting new patient – limit to 90mg ME
8. Patients on >90mg ME and not doing well – rotate or taper
9. Patients on >90mg ME – taper as low as possible
10. Difficulty tapering patients → Multi-D taper program

Red = strong, Blue = weak

http://nationalpaincentre.mcmaster.ca/guidelines.html
When would you consider opioid therapy?

Recommendation 2: For patients with chronic noncancer pain, without current or past substance use disorder and without other active psychiatric disorders, who have persistent problematic pain despite optimized nonopioid therapy.

We suggest adding a trial of opioids rather than continued therapy without opioids.

By a trial of opioids, we mean initiation, titration, and monitoring of response, with discontinuation of opioids if important improvement in pain or function is not achieved. The studies that identified substance use disorder as a risk factor for adverse outcomes characterized the conditions as alcohol abuse and dependence, and narcotic abuse and dependence, and sometimes referred to ICD-9 diagnoses. The mental illnesses identified in studies as risk factors for adverse outcomes were generally anxiety and depression, including ICD-9 definitions, as well as “psychiatric diagnosis”, “mood disorder”, and post-traumatic stress disorder.
Initiating an Opioid

- BPI assessment tool
- ORT
- Urine drug testing at baseline
- Opioid agreement
- Controlled dispensing intervals
- Trial of therapy – ensure improved function and decreased pain with minimal side effects
- Boundaries for everyone!

Brief Pain Inventory - BPI

Adapted from Cleeland CS, Ryan KM, 1994.
Pain Agreement

- Single prescriber
- Single pharmacy
- No missed appt
- No recreational drugs (alcohol)
- No OTC opioids/ cough syrups?
- Body fluid testing as necessary
- Freedom of information
- Risk of Addiction
Recommendations 6 and 7: For patients with chronic noncancer pain who are beginning long term opioid therapy

**Strong Recommendation**

Recommendation 6: We recommend restricting the prescribed dose to less 90mg morphine equivalents daily rather than no upper limit or a higher limit on dosing.

*Some patients may gain important benefit at a dose of more than 90mg morphine equivalents daily. Referral to a colleague for a second opinion regarding the possibility of increasing the dose to more than 90mg morphine equivalents daily may therefore be warranted in some individuals.*

**Weak Recommendation**

Recommendation 7: For patients with chronic noncancer pain who are beginning opioid therapy, we suggest restricting the prescribed dose to less than 50mg morphine equivalents daily.

*The weak recommendation to restrict the prescribed dose to less than 50mg morphine equivalents daily acknowledges that there are likely to be some patients who would be ready to accept the increased risks associated with a dose higher than 50mg in order to potentially achieve improved pain control.*
Which Opioid?

Are there some pain problems that are less likely to respond to opioids?
Mechanistic Characterization of Pain

**Nociceptive (Structural)**
- Inflammation or mechanical damage in tissues
- Classic examples:
  - Acute pain due to injury
  - Osteoarthritis
  - Rheumatoid arthritis
  - Cancer pain

**Neuropathic**
- Damage or dysfunction of within the nervous system
- Classic examples:
  - Diabetic neuropathic pain
  - Post-herpetic neuralgia
  - Central stroke syndrome

**Centralized Pain**
- Characterized by central disturbance in pain processing (diffuse hyperalgesia/allodynia)
- Classic examples:
  - Fibromyalgia
  - Irritable bowel syndrome
  - TMJ D
  - Tension headache

Clauw IASP 2016

---

Treating Pain Based on Mechanisms

*any combination may be present*

<table>
<thead>
<tr>
<th></th>
<th>Peripheral Pain (nociceptive)</th>
<th>Neuropathic Pain</th>
<th>Centralized Pain</th>
</tr>
</thead>
<tbody>
<tr>
<td>NSAIDs</td>
<td>+</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Opioids</td>
<td>+</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>Surgery/Injections</td>
<td>+</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>Tricyclics</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>SNRIs</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Gabapentinoid</td>
<td>-</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Cannabinoid</td>
<td>-</td>
<td>+</td>
<td>+</td>
</tr>
</tbody>
</table>

Clauw IASP 2016
Traditional Opioids

- Morphine
- Hydromorphone
- Oxycodone
- Fentanyl
- Codeine

Novel Opioids

- Tramadol
- Tapentadol
- Methadone
- Ketamine
- Buprenorphine
When to Consider Tapering Opioid Therapy

- Patient request
- Pain condition resolved
- Risks outweigh benefits
  - Repeated out of bounds behaviours — ? OUD
- Adverse effects outweigh benefits
  - High-risk behaviours for overdose
  - ? Opioid hyperalgesia
- Medical complications
- Opioid not effective
  - No improvement in function / QOL
- (?Regulatory “suggestion”?)

2017 Opioid Guidelines
Recommendation #9 (weak)

For patients currently using 90 mg morphine equivalents of opioids per day or more

We suggest tapering opioids to the **lowest effective dose**, potentially including discontinuation, rather than no change in opioid therapy

Some patients are likely to experience significant increase in pain or decrease in function that persists more than one month after a small dose reduction; **tapering may be paused and potentially abandoned in such patients**.

http://nationalpaincentre.mcmaster.ca/guidelines.html
**Tapering Opioid Therapy**

1. Discuss and document (with significant other):
   - Withdrawal is not dangerous to most people
   - Typical withdrawal symptoms and time course
2. Offer an alternative treatment plan
3. Careful with sedatives – withdrawal is more risky

Patients who are diverting or addicted may refuse to comply and leave your practice

**Risks of Opioid Withdrawal**

Careful:

- Pregnancy
- Fragile medical or psychiatric condition
- Severe SUD
  - Risk of relapse → loss of tolerance → overdose
Tapering Opioids

- Fast or slow
  - Pharmacy dispensing
  - 10% per week – ? blister packing
  - 10% per month
  - When down to 1/3 of total dose – consider slower reduction (5%)
- Use pharmacological aids
  - Clonidine, Imodium, NSAID, PGN, Nabilone, Gabapentin, CPZ
- Methadone (buprenorphine) taper
- Talking to the patient is the most effective treatment!

What About Benzodiazepines?
Benzodiazepines – Benign Drugs?

- Among the most common prescribed drugs in Canada
- Most are indicated for short term use only
- Often used to treat “stress”
- Significant issues with long term use including cognitive dysfunction, recurrent falls and death
- Increase the risk of AD by two fold
- When combined with opioids increase the risk of accidental death
- Difficult to get off once on – Protracted BDZ Withdrawal Syndrome
“Dose-response associations were found for all three classes of study drugs (benzodiazepines, Z drugs (zaleplon, zolpidem, and zopiclone), and other drugs). After excluding deaths in the first year, there were approximately four excess deaths linked to drug use per 100 people followed for an average of 7.6 years after their first prescription.”

---

**Benzodiazepine Tapering**

1. **Benefits of Benzodiazepine Tapering**
   - Lower the risk of future adverse drug-related risks such as falls and cognitive impairment
   - Increased alertness and energy

2. **Approach to Tapering**
   - Taper slowly: slow tapers are more likely to be successful than fast tapers
   - Use scheduled rather than p.r.n. doses
   - Halt or reverse taper if severe anxiety or depression occurs
   - Schedule follow-up visits q 1-4 weeks depending on the patient’s response to taper
   - At each visit, ask patient about the benefits of tapering (e.g., increased energy, increased alertness)

Adapted from Kahan 2002; Appendix B-6: Benzodiazepine Tapering. Available at: http://nationalpaincentre.mcmaster.ca/opioid/
**Decreasing the Dose**
- Taper by no more than 5 mg diazepam equivalent per week.
- Adjust rate of taper according to symptoms.
- Slow the pace of the taper once dose is below 20 mg of diazepam equivalent (e.g., 1–2 mg/week).
- Instruct the pharmacist to dispense daily, twice weekly, or weekly depending on dose and patient reliability.

**Another Approach**
- Taper according to the proportional dose remaining: Taper by 10% of the dose every 1–2 weeks until the dose is at 20% of the original dose; then taper by 5% every 2–4 weeks.

*Source: Adapted from Kahan 2002.*

<table>
<thead>
<tr>
<th>Benzodiazepine</th>
<th>Equivalent to 5 mg diazepam (mg) *</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alprazolam (Xanax®)**</td>
<td>0.5</td>
</tr>
<tr>
<td>Bromazepam (Lectopam®)</td>
<td>3–6</td>
</tr>
<tr>
<td>Chlordiazepoxide (Librium®)</td>
<td>10–25</td>
</tr>
<tr>
<td>Clonazepam (Rivotril®)</td>
<td>0.5–1</td>
</tr>
<tr>
<td>Clorazepate (Tranxene®)</td>
<td>7.5</td>
</tr>
<tr>
<td>Flurazepam (Dalmane®)</td>
<td>15</td>
</tr>
<tr>
<td>Lorazepam (Ativan®)</td>
<td>0.5–1</td>
</tr>
<tr>
<td>Nitrazepam (Mogadon®)</td>
<td>5–10</td>
</tr>
<tr>
<td>Oxazepam (Serax®)</td>
<td>15</td>
</tr>
<tr>
<td>Temazepam (Restoril®)</td>
<td>10–15</td>
</tr>
<tr>
<td>Triazolam (Halcion®)**</td>
<td>0.25</td>
</tr>
</tbody>
</table>
What About Intervventional Therapies?

- Chronic pain cannot be imaged
- Target injections on clinical exam and not radiologist report
- Multiple options for injections including cortisone, viscosupplementation, PRP and adult stem cells.
- Cortisone be done safely every 3 – 6 months in most patients - concerns if a history of untreated osteoporosis
- Only should be done to enhance rehabilitation and NOT as a solely therapeutic intervention

Back to the Cases...

- GS opioids not helping and may be making her worse. HMC was tapered and her pains became more localized. Feeling better but still has pain. Currently trialing CBD oil
- RL doing well on current opioids. Opioids continued with regular monitoring every 3 months including functional assessments, monthly dispensing of medications and urine drug screening.
“It was the age of wisdom, it was the age of foolishness…”

- Charles Dickens
I hope you learned something...

QUESTIONS?