Prescription Opioid Addiction

Presentation provided by Meldon Kahan, MD
Family & Community Medicine
University of Toronto
Conflict of interest statement

- I received funds from Rickett Benkeiser to present on Suboxone (buprenorphine)
The Opioid Crisis

- Very serious (overdose deaths = deaths from MVA)
- Iatrogenic: MD prescriptions are the major source of opioids, directly or through diversion
4x increase in prescribing of strong opioids

Dhalla et al CMAJ 2009
9x increase in oxycodone-related deaths

Before addition of OxyContin onto public drug formulary

After addition of OxyContin onto public drug formulary

Dhalla et al. CMAJ 2009
Details of 423 Ontario deaths in 2006

<table>
<thead>
<tr>
<th>Manner of death</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Accident</td>
<td>285 (67%)</td>
</tr>
<tr>
<td>Suicide</td>
<td>65 (15%)</td>
</tr>
<tr>
<td>Undetermined</td>
<td>71 (17%)</td>
</tr>
<tr>
<td>Other or missing</td>
<td>2 (0%)</td>
</tr>
</tbody>
</table>

**Opioids associated with death**

<table>
<thead>
<tr>
<th>Single opioid</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Oxycodone</td>
<td>119 (40%)</td>
</tr>
<tr>
<td>Morphine or heroin (or both)</td>
<td>66 (22%)</td>
</tr>
<tr>
<td>Methadone</td>
<td>55 (19%)</td>
</tr>
<tr>
<td>Fentanyl</td>
<td>14 (5%)</td>
</tr>
<tr>
<td>Codeine</td>
<td>10 (3%)</td>
</tr>
<tr>
<td>Other</td>
<td>33 (11%)</td>
</tr>
</tbody>
</table>
Most deaths occur in people who were prescribed opioids

- 56% dispensed an opioid in the 4 weeks prior to death
- 82% dispensed an opioid in the year prior to death
- Median number of opioid prescriptions in year prior to death
  → 10 prescriptions

Important limitation: data only available for 1/3 of population (those eligible for public coverage)
Case-control study: opioid dose & risk of OD

<table>
<thead>
<tr>
<th>Dose (mg morphine equivalent/day)</th>
<th>Odds Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt; 200 mg</td>
<td>2.9</td>
</tr>
<tr>
<td>100-199 mg</td>
<td>2.0</td>
</tr>
<tr>
<td>50-99 mg</td>
<td>1.9</td>
</tr>
<tr>
<td>20-49 mg</td>
<td>1.3</td>
</tr>
</tbody>
</table>
Rise in prescription opioid addiction

Figure 1. Admissions to the Medical Withdrawal Management Service for opioid detoxification, 2000–2004: The number of admissions increased over the 5 years (2000, n = 78; 2001, n = 96; 2002, n = 120; 2003, n = 111; and 2004, n = 166). Of the 571 admissions, 295 involved 1 opioid, 204 involved 2 opioids, 68 involved 3 opioids, and 4 involved 4 opioids.

Sproule B et al Can Fam Phys 2009
Number of patients on opioids causing concerns

Wenghofer 2010

<table>
<thead>
<tr>
<th>Number of Patients Causing Concerns for FP</th>
<th>Percent of FPs (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>None</td>
<td>15.1</td>
</tr>
<tr>
<td>1 – 3</td>
<td>47.9</td>
</tr>
<tr>
<td>4 – 6</td>
<td>23.4</td>
</tr>
<tr>
<td>7 – 9</td>
<td>6.4</td>
</tr>
<tr>
<td>10 or more</td>
<td>7.2</td>
</tr>
</tbody>
</table>
FPs very concerned about...

<table>
<thead>
<tr>
<th>Concerns</th>
<th>Very concerned (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Running out early, demanding fit-in appointments, lost scripts</td>
<td>44.8</td>
</tr>
<tr>
<td>Lack of specialized pain clinics</td>
<td>42.2</td>
</tr>
<tr>
<td>Getting patient addicted (n=641)</td>
<td>38.4</td>
</tr>
<tr>
<td>Patients getting high doses</td>
<td>28.0</td>
</tr>
<tr>
<td>Lack of addiction treatment resources</td>
<td>26.4</td>
</tr>
<tr>
<td>Disagreements with patients about opioids</td>
<td>22.0</td>
</tr>
</tbody>
</table>
ADDICTION: KEY CONCEPTS
Addiction: Clinical Features

- Repeated drug reinforcement -> patient has trouble controlling use
- Opioids & all drugs of abuse acts on ‘reward centre’ – medial forebrain bundle
- Tolerance and withdrawal develop quickly
Addiction (2): 4 Cs of Addiction

- Compulsive drug use
- Craving
- Consequences: Use despite harm
- Inability to Cut down
Tolerance

- Neurobehavioural adaptation
- Tolerance to analgesic effects develops slowly
- Rapid tolerance to psychoactive effects
- Highly tolerant patients can function on massive amounts of opioids
- Tolerance disappears within days
Withdrawal

- Usually mild, transient in patients taking moderate doses for analgesia
- More severe in patients taking higher doses for psychoactive effects
- No serious medical complications, except in pregnant women and neonates
Withdrawal: Time Course

- Begins 6-24 hours after last use
- Peaks at 2-3 days
- Physical symptoms largely resolve by 5-10 days
- In severe withdrawal, insomnia and dysphoria may last weeks-months
Withdrawal: Symptoms

Psychological:
- Intense anxiety
- Craving for opiates
- Restlessness, insomnia, fatigue

Physical:
- Myalgias
- Nausea, vomiting, cramps, diarrhea, sweating
- Signs (not usually seen): Agitation, dilated pupils, chills, goosebumps
Withdrawal-mediated Pain

- Pain magnified as opioid wears off
- Pain “all over” (myalgia)
- Dysphoria
- Symptoms quickly relieved with opioids
**Prescription Opioid Addiction**

**Most pain patients don’t become addicted:**
- Tolerance to analgesic effects develops slowly
- Patients often remain on same dose for years
- Most do not experience euphoria
PRESCRIPTION OPIOID ADDICTION: PREVENTION
Prevalence of Addiction to Prescription Opioids

- Recent meta-analysis: 3% in pain patients
- 14% show aberrant drug behaviours
- Usually associated current/past history of substance dependence

Fishbain 2008
Prevalence of Opioid Abuse and Addiction

- Rates of prescription opioid abuse and addiction are increasing rapidly
- Based on data from surveys of general population, high school students, drug overdoses, methadone programs
Major cause of the increase...

- Prescribing higher doses of opioids to greater numbers of high risk people
- High risk patients more likely to experience euphoria or anxiety relief with opioids
  - This may lead to tolerance, dose escalation, withdrawal and addiction
- Euphoric and anxiolytic effects of opioids are dose related
Cause of crisis (2)

- Addiction risk of high opioid doses not counterbalanced by better pain relief:
  - Other complications of opioids are also dose related (overdose, sleep apnea etc)
  - The effectiveness of high opioid doses has not been demonstrated
  - Patients receiving high doses have milder biomedical pain conditions, are younger and have greater psychiatric comorbidity
Prevention

- Don’t prescribe opioids to high risk patients (younger, male, personal or strong family hx of addiction, active psychiatric disorder) unless:
  - Has condition for which opioids shown to improve functional status (generally NOT low back pain or fibromyalgia)
  - Failed trial of first line medications and non-medical approaches
Prevention (2)

- If opioids are used, titrate slowly with codeine/tramadol first
- Avoid hydromorphone
- Keep maintenance dose << 200 mg MED
- Taper if dose above this
- Careful monitoring for aberrant behaviour and UDS
When to taper

- Severe pain and poor function despite high dose
- Complication: Depression, fatigue, sleep apnea, sexual dysfunction, falls
- High dose may no longer be necessary
- Addiction – discussed later
How to taper

- Explain that tapering improves pain, mood and function
  - During taper, ask about positive effects not just withdrawal
- Use scheduled doses
  - Frequent dispensing with no early refills
- Taper by no more than 10% of dose q 2 weeks
- Negotiate with patient re rate of taper
- Endpoint not necessarily abstinence
- Also taper benzodiazepines
PRESCRIPTION OPIOID ADDICTION: DIAGNOSIS
Addiction: Typical history

- Current, past or family history of addiction
- On a high dose for underlying pain condition
- Strong resistance to changing opioid
- Reports severe pain, little evidence of benefit from opioid
- Withdrawal symptoms
- Depression, irritability, anxiety
- Social isolation, deteriorating functioning

Canadian Society of Addiction Medicine
La Société Médicale Canadienne sur l’Addiction
Laboratory Findings

- Elevated AST, ALT (viral or alcoholic hepatitis)
- Gamma GT, MCV (alcohol)
- Hepatitis B, C
Other Sources of Information

- Often critical
- Addiction is longitudinal diagnosis
  - Other physicians
  - Spouse, family
Behaviours

- Binge use (“unsanctioned dose escalations”)
- Alters route of entry
  - bite, crush, snort, inject
- Accesses opioids from other sources
  - Other doctors, the ‘street’
Why do they act like this?

- Overcome tolerance
- Achieve psychoactive effect
- Avoid withdrawal
Limitations of behaviour monitoring

- Patients will hide these behaviours
- These behaviours not always seen if physician prescribes higher doses
- Some patients take oral opioids without running out early yet experience psychoactive effects, withdrawal, dysphoria and decreased function
Urine Drug Screening

- Pain patients have high prevalence of unauthorized drug use on UDS
- Patients usually don’t object if it’s routine
- Used for detection of:
  - Diversion and non-compliance
  - Double-doctoring
  - Abuse of other drugs eg cocaine, benzodiazepines
Types of UDS: Immunoassay

- Opioids, cocaine, benzodiazepines etc.
- Detects use for up to five days
- False +ve: Poppy seeds
- False –ve:
  - Often misses semisynthetic opioids (oxycodone)
  - Usually misses synthetic opioids (methadone, fentanyl)
Chromatography

- Detects specific opioids
- Shorter window of detection (1-2 days)
- More sensitive for oxycodone & other synthetics
- Codeine metabolized to morphine
Limitations

- Not quantitative
- Easy to tamper
- Influenced by a variety of factors
- False +ve, -ve common

To order:
- Specify drugs you wish to detect
- Or specify “broad spectrum” toxicology
PRESCRIPTION OPIOID ADDICTION: TREATMENT
Management of Suspected Opioid addiction

- Trial of structured opioid therapy
- Methadone or buprenorphine
- Abstinence-based treatment
Structured opioid therapy: Indications

- Has biomedical pain condition that hasn’t responded to non-opioid therapy
- Is not injecting or crushing opioids
- Is not acquiring opioids from other sources
- Is not currently abusing other drugs
  - Limited evidence of effectiveness so view as therapeutic trial
Structured opioid therapy

- Frequent visits, regular UDS, faxed scripts
- Daily or alternate day dispensing
- Long-acting scheduled opioids
- Avoid opioids with higher addiction liability eg hydromorphone
- Taper if on high dose (> 200 mg MED)
Methadone treatment: Indications

- Failed trial of structured opioid therapy
- Injecting or crushing tablets
- Double doctoring or acquiring opioids from other sources
- Currently addicted to other drugs
Methadone treatment

- Slow onset, long duration of action
- Relieves withdrawal, cravings without sedation or euphoria
- Can be monitored with UDS
Methadone Rx (2)

- Three components:
  - Daily dispensing with gradual introduction of take-home doses
  - Regular UDS
  - Counselling and medical care
- Provincial College guidelines about methadone Rx
  - who prescribes & how
Limitations of methadone treatment

- High risk of overdose early in treatment
  - Optimal candidate is highly tolerant to opioids
- Not all communities have methadone providers
- Major commitment of time for patient and provider
Buprenorphine

- Suboxone (buprenorphine + naloxone)
- Sublingual partial opioid agonist
- Long duration of action
- As effective as 60-80 mg of methadone
- Lower risk of overdose than methadone (ceiling effect because partial agonist)
Buprenorphine: ODB criteria

- Three-month wait for methadone Rx
- Methadone failed or contraindicated
- High risk for toxicity
  - > 65
  - Not fully opioid tolerant eg codeine or binge user
  - Heavy drinker
  - Benzodiazepine use
  - COPD
Abstinence-based treatments

- Medical detoxification
  - Buprenorphine, clonidine, opioid tapering, methadone tapering
  - Usually fails with heroin users but may be more effective with prescription use
- NA, AA, self-help groups
- Naltrexone (opioid antagonist)
- Residential or outpatient treatments
Addiction and pain: Paradigm shift

- MDs see pain treatment is in opposition to addiction treatment
  - ‘Patient is addicted but also has severe pain – if I stop opioids his/her pain will be unbearable’
- Yet evidence shows this is false:
  - Opioid addiction increases pain perception and depression, worsens function
  - Patient’s pain, mood and functioning improves with treatment, by resolving withdrawal-mediated pain and opioid-induced depression
What if patient refuses to enter treatment?

- If you’re prescribing the opioid:
  - Explain that ongoing opioid prescribing is unsafe and will make patient feel worse
  - Pain, mood and function improves with treatment

- Give a firm start date for treatment: Structured opioid therapy, methadone or buprenorphine

- If patient refuses, taper and discontinue BUT do not ‘fire’ the patient