Opioids and Chronic Pain

CRIT/FIT 2013

May 2013

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Assistant Dean, Continuing Medical Education

Boston University School of Medicine
Bad News and Good News

• **Bad News:**
  – I changed my talk

• **Good News:**
  – It is a better talk
  – You will get the better talk on your USB drive

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Four Powerful Learning Experiences

1. A patient being admitted to a methadone maintenance program

2. A walk down the hall to my first Medical Grand Rounds presentation with the Chair of Medicine

3. A conversation with my aunt Harriet

4. A complement from a primary care patient
My Biases

• Opioids...
  • can be effective for some
  • can be harmful for some
  • can be prescribed safely

• Providers **can be** and **want to be** trained to prescribe opioids for chronic pain safely and competently
Opioid Sales, Deaths and Addiction Treatment Admissions

The Problem... chronic pain is complicated

Variables Affecting Pain Experience

Genetic predispositions
- Structure and function of the nervous system
- Molecular basis for response to pain and/or analgesic

Environmental stressor effects
- Work, home

Social and cultural beliefs effects
- Socially determined constructs of pain, suffering and disability
- Beliefs about pain treatment

Psychiatric Co-mobidities
Chronic Pain is Complicated

- Cultural Background
- Environmental Stressors
- Physical Injury
- Genetics
- Cognitive Dysfunction
- Depression & Anxiety
- Functional Disability
- Social Disability

Patient “A” Pain 8/10

Gatchel RJ. Am Psychol. 2004
More UNREALISTIC expectations...

Opioids always = Pain relief

therefore

More opioids = More pain relief
Opioid Efficacy in Chronic Pain

- Most literature surveys & uncontrolled case series
- RCTs are short duration <8 months w/ small samples <300 pts

While we all want better evidence...

Absence of evidence is NOT evidence of absence

- Addiction not assessed

Balantyne JC, Mao J. NEJM 2003
Kalso E et al. Pain 2004
Eisenberg E et al. JAMA. 2005
Furlan AD et al. CMAJ 2006

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Neuropathic Pain

<table>
<thead>
<tr>
<th>Medication</th>
<th>NNT</th>
<th>NNH</th>
</tr>
</thead>
<tbody>
<tr>
<td>TCA</td>
<td>2.1</td>
<td>15.9</td>
</tr>
<tr>
<td>Opioids</td>
<td>2.6</td>
<td>17.1</td>
</tr>
<tr>
<td>Pregabalin</td>
<td>4.5</td>
<td>10.6</td>
</tr>
<tr>
<td>Tramadol</td>
<td>4.9</td>
<td>13.3</td>
</tr>
<tr>
<td>SNRI</td>
<td>5.0</td>
<td>13.1</td>
</tr>
<tr>
<td>Gabapentin</td>
<td>6.4</td>
<td>32.5</td>
</tr>
<tr>
<td>SSRI</td>
<td>6.8</td>
<td>-</td>
</tr>
</tbody>
</table>

Finnerup NB et al. Pain. 2010
Opioid Efficacy in Chronic Pain

Proportion of Patients with at least 50% Pain Relief, Oral Opioids, Follow-up 7.5 months (mean) to 13 months ($I^2=77.3\%$)

<table>
<thead>
<tr>
<th>Study Name</th>
<th>Statistics for each study</th>
<th>Proportion</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>Event rate</td>
<td>Lower limit</td>
</tr>
<tr>
<td>Zenz 1992</td>
<td>0.510</td>
<td>0.413</td>
</tr>
<tr>
<td>Allan 2005</td>
<td>0.392</td>
<td>0.341</td>
</tr>
<tr>
<td></td>
<td>0.443</td>
<td>0.333</td>
</tr>
</tbody>
</table>

- N=442
- 44.3% of participants had at least 50% pain relief
The Problem...variable opioid response

Mu Receptor

- G protein-coupled receptor family, signal via second messenger (cAMP)
- Mu receptor subtypes
- >100 polymorphisms in the human MOR gene

Opioid metabolism

- Differs by individual opioid and by individual patient

- Not all chronic pain responds to opioids
- Not all pain responds to same opioid in the same way
- Trial of several opioids may be needed to find acceptable balance between analgesia and tolerability

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## Issues Preventing Opioid Prescribing

### n=111

<table>
<thead>
<tr>
<th>Issue</th>
<th>Percentage</th>
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</thead>
<tbody>
<tr>
<td>Potential for patients to become addicted</td>
<td>89%</td>
</tr>
<tr>
<td>Potential for patients to sell or divert</td>
<td>75%</td>
</tr>
<tr>
<td>Opioid side effects</td>
<td>53%</td>
</tr>
<tr>
<td>Regulatory/law enforcement monitoring</td>
<td>40%</td>
</tr>
<tr>
<td>Hassle and time required to track/refill</td>
<td>28%</td>
</tr>
</tbody>
</table>

Upshur CC et al. J Gen Intern Med 2006
Opioid Misuse/Addiction Risk

- Published rates of abuse and/or addiction in chronic pain populations are 3-19%
- **Known risk factors** for addiction to any substance are **good predictors** for problematic prescription opioid use
  - Young age
  - Personal history of substance abuse
    - Illicit, prescription, alcohol, nicotine
  - Family history of substance abuse
  - Legal history (DUI, incarceration)
  - Mental health problems

Akbik H et al. JPSM 2006
Ives T et al. BMC Health Services Research 2006
Liebschutz JM et al. J of Pain 2010
Michna E et al. JPSM 2004
Reid MC et al JGIM 2002
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Overdose Risk

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Percentage of patients and prescription drug overdoses, by risk group

- Patients seeing multiple doctors and typically involved in drug diversion
- Patients seeing one doctor, high dose
- Patients seeing one doctor, low dose

Is my patient “pain-relief seeking” or “drug seeking” or both?

- There are no “pain meters”
- Vital signs are not reliable in chronic pain
- Pain is subjective to the patient and to the provider
- It is difficult to distinguish *inappropriate* drug-seeking from *appropriate* pain relief-seeking or *both* on the first visit (s)
Is the my patient addicted?

- Physical dependence
  - Biological adaptation
  - Signs and symptoms of withdrawal (e.g., pain) if opioid is abruptly stopped

- Addiction (4 C’s)
  - Behavioral maladaptation
  - Loss of Control
  - Compulsive use
  - Continued use despite harm
  - Craving

- Opioid Dependence (DSM IV)
  - Behavioral maladaptation +/- Biological

Aberrant Medication Taking Behaviors (Pattern & Severity)

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Aberrant Medication Taking Behaviors

The Spectrum of Severity

- Requests for increase opioid dose
- Requests for specific opioid by name, “brand name only”
- Non-adherence w/ other recommended therapies (e.g., PT)
- Running out early (i.e., unsanctioned dose escalation)
- Resistance to change therapy despite AE (e.g. over-sedation)
- Deterioration in function at home and work
- Non-adherence w/ monitoring (e.g. pill counts, urine drug tests)
- Multiple “lost” or “stolen” opioid prescriptions
- Illegal activities – forging scripts, selling opioid prescription

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Aberrant Medication-Taking Behaviors

Differential Diagnosis

Pain Relief Seeking
- Disease progression
- Poorly opioid responsive pain
- Withdrawal mediated pain
- Opioid analgesic tolerance
- Opioid-induced hyperalgesia

Drug Seeking
- Addiction
- Other psychiatric diagnosis
- Criminal intent (diversion)

Alford DP. JAMA 2013
When Are Opioids Indicated?

• Pain is moderate to severe
• Pain has significant impact on function and on quality of life
• Non-opioid pharmacotherapy has been tried and failed
• Patient agreeable to...
  – take opioid as prescribed (e.g. no dose escalation)
  – close monitoring (e.g. pill counts, urine drug testing)
Opioid Safety

- **Allergies** are rare
- **Adverse effects** are common
  - Nausea, **sedation**, constipation
  - Urinary retention, sweating, **respiratory depression**
- **Organ toxicities** are rare
  - Hypothalamic-pituitary-gonadal axis - ↑prolactin, ↓ LH, FSH, testosterone, estrogen, progesterone
- **Overdose** especially when combined w/ other sedatives

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Opioid Choice

- Duration and onset of action
  - “Rate hypothesis” - fast on, fast off – most rewarding – addicting
  - Short-acting opioids increase risk of opioid-withdrawal mediated pain

- Patient’s prior experience
  - *Mu* polymorphisms – differences in opioid responsiveness

- **Currently there are NO proven abuse resistant opioids or opioid formulations!!**
Key Principles

• Maintain benefit-risk (harm) framework

• Judge the treatment NOT the patient
Assessing Benefit - Risk/Harm
“Universal Precautions”
(not evidence-based but has become “standard” of care)

- Agreements “contracts”, informed consent
- Monitor for benefit and harm with frequent face-to-face visits
- Monitor for adherence, addiction and diversion
  - Urine drug testing
  - Pill counts
  - Prescription monitoring program data

FSMB Guidelines 2004 www.fsmb.org
Gourlay DL, Heit HA. Pain Medicine 2005
Chou R et al. J Pain 2009
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### Assessing Benefit: PEG scale

1. What number best describes your pain on average in the past week:

<table>
<thead>
<tr>
<th>0</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
<th>8</th>
<th>9</th>
<th>10</th>
</tr>
</thead>
<tbody>
<tr>
<td>No pain</td>
<td>Pain as bad as you can imagine</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<td></td>
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</tbody>
</table>

2. What number best describes how, during the past week, pain has interfered with your enjoyment of life?

<table>
<thead>
<tr>
<th>0</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
<th>8</th>
<th>9</th>
<th>10</th>
</tr>
</thead>
<tbody>
<tr>
<td>Does not interfere</td>
<td>Completely interferes</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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</tbody>
</table>

3. What number best describes how, during the past week, pain has interfered with your general activity?

<table>
<thead>
<tr>
<th>0</th>
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<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
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<th>10</th>
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</tbody>
</table>

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## Assessing Risk: Opioid Risk Tool

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Female</th>
<th>Male</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Family history of substance abuse</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Alcohol</td>
<td>☐1</td>
<td>☐3</td>
</tr>
<tr>
<td>Illegal drugs</td>
<td>☐2</td>
<td>☐3</td>
</tr>
<tr>
<td>Prescription drugs</td>
<td>☐4</td>
<td>☐4</td>
</tr>
<tr>
<td><strong>Personal history of substance abuse</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Alcohol</td>
<td>☐3</td>
<td>☐3</td>
</tr>
<tr>
<td>Illegal drugs</td>
<td>☐4</td>
<td>☐4</td>
</tr>
<tr>
<td>Prescription drugs</td>
<td>☐5</td>
<td>☐5</td>
</tr>
<tr>
<td><strong>Age between 16-45 years</strong></td>
<td>☐1</td>
<td>☐1</td>
</tr>
<tr>
<td><strong>History of preadolescent sexual abuse</strong></td>
<td>☐3</td>
<td>☐0</td>
</tr>
<tr>
<td><strong>Psychological disease</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ADHD, OCD, bipolar, schizophrenia</td>
<td>☐2</td>
<td>☐2</td>
</tr>
<tr>
<td>Depression</td>
<td>☐1</td>
<td>☐1</td>
</tr>
</tbody>
</table>

### Scoring
- 0-3 low risk
- 4-7 moderate risk
- >8 high risk

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Webster LR, Webster RM. Pain Medicine, 2006
Discussing Monitoring with Patients

- Discuss risks of opioid medications
- Assign responsibility to look for early signs of harm
- Discuss agreements, pill counts, drug tests, etc. as ways that you are helping to protect patient from getting harmed by medications
  - Thiazide diuretic - K monitoring analogy
- Use consistent approach, but set **level of** monitoring to match risk
Monitoring

Urine Drug Tests

• Evidence of therapeutic adherence

• Evidence of non-use of illicit drugs

• Know limitations of test and your lab

• Know a toxicologist/clinical pathologist

• Complex, but necessary, patient-physician communication
  – If I send your urine right now, what will I find in it...
  – Your urine drug test was abnormal, can you tell me about it...

• Document time of last medication use

• Inappropriate interpretation of results may adversely affect clinical decisions

• Confirm medication adherence
• Minimize diversion
• My strategies...
  – 28 day (rather than 30 day) supply
  – All patients expected to bring remaining pills at each visit
    • If patient “forgets” pills, schedule return visit with in a week
  – For “high risk” patient, use random call-backs
Continuation of Opioids

• You must convince yourself that there is benefit

• Benefit must outweigh observed harms

• If small benefit, consider increasing dose as a "test".

• If no benefit, hence benefit cannot outweigh risks – so STOP opioids. (Ok to taper and reassess.)

• You do not have to prove addiction or diversion – only assess Risk-Benefit ratio
Exit Strategy
Discussing Lack of Benefit

- Stress how much you believe / empathize with patient’s pain severity and impact
- Express frustration re: lack of good pill to fix it
- Focus on patient’s strengths
- Encourage therapies for “coping with” pain
- Show commitment to continue caring about patient and pain, even without opioids i.e., you are abandoning (discharging) an ineffective treatment, **not** the patient
- Schedule close follow-ups during and after taper

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Exit Strategy
Discussing Possible Addiction

• Give specific and timely feedback why patient’s behaviors raise your concern for possible addiction

• Benefits no longer outweighing risks
  – “I cannot responsibly continue prescribing opioids as I feel it would cause you more harm than good.”

• Always offer referral to addiction treatment

• Stay 100% in “Benefit/Risk of Med” mindset

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Summary

- Opioids can be effective and safe but are imperfect
- Use risk/harm - benefit framework
- Use consistent approach, but set level of monitoring to match risk
- Judge the treatment and not the patient
- If there is benefit in the absence of harm, continue opioids
- If there is no benefit or if there is harm, discontinue opioids

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Two FREE Online Educational Resources

www.scopeofpain.com

www.opioidprescribing.com
Safe and Competent Opioid Prescribing Education (SCOPE) Program

Risk Evaluation and Mitigation Strategy (REMS) Program

• 3 components
  – *Free* 3 module web-based education
  – 10 Live conference held around the US
    • MA, MI, NE, NC, OR, RI, WI
  – Train-the-trainer workshops

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Module 2: Second Visit - One Week Later Initiating Opioid Therapy Safely

Web-based Program

3 Modules
How to:
- determine when opioid analgesics are indicated
- assess for opioid misuse risk
- talk to patients about opioid risks and benefits
- monitor and manage patients on long-term opioid therapy

Case Study: Mary Williams
- 42 year old female
- Hypertension
- Type 2 diabetes with painful neuropathy
- Chronic low back pain

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