Session 12: Responsible Opioid Prescribing in 2012

Learning Objectives

1. Before initiating opioid therapy, obtain a comprehensive patient history to determine whether the patient may be at increased risk for opioid abuse.

2. Assess the most frequently encountered clinical and behavioral adverse effects of opioid therapy to incorporate into ongoing monitoring protocols in order to ensure patients are adhering to individualized treatment plans.
Session 12

Responsible Opioid Prescribing in 2012

Faculty

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Dr Salsitz is a course director for the American Society of Addiction Medicine (ASAM)–sponsored buprenorphine trainings and a participating physician in the Physician Clinical Support System (PCSS) mentoring program, both for buprenorphine and opioids. He is a co-chair of the ASAM Review, Common Threads, and State-of-the-Art courses, and a reviewer for the Journal of Addiction Medicine. Dr Salsitz is also co-chair of the ASAM continuing medical education (CME) committee and chair of the New York Society of Addiction Medicine (NYSAM) CME and education committee.

Dr Salsitz is a member of the medical advisory panel of the New York State Office of Alcohol and Substance Abuse Services (OASAS).

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Learning Objectives

- Before initiating opioid therapy, obtain a comprehensive patient history to determine whether the patient may be at increased risk for opioid abuse
- Assess the most frequently encountered clinical and behavioral adverse effects of opioid therapy to incorporate into ongoing monitoring protocols in order to ensure patients are adhering to individualized treatment plans

Q1. Pre-Activity Audience Response Question

Long-term efficacy of opioids for chronic non-cancer pain has been well established.

1. True
2. False
3. Not sure

Q2. Pre-Activity Audience Response Question

Patient risk factors for opioid abuse include:

1. Age > 45 years
2. History of childhood obesity
3. History of depression
4. All of the above

Q3. Pre-Activity Audience Response Question

Which of the following is TRUE regarding extended-release/long-acting (ER/LA) opioids?

1. A patient should not start on an ER/LA opioid regimen if already opioid tolerant
2. Overdose from transdermal preparations can occur if the patient becomes febrile
3. ER/LA opioids are less addictive than short-acting opioids
4. All of the above
1. Pharmacology of Opioids

Types of Opioid Receptors

1. Mu
2. Kappa
3. Delta

Opioid Medications

1. Naturally Occurring Opioids
   - Morphine
   - Codeine

2. Semi-Synthetic Opioids
   - Oxymorphone
   - Oxycodone
   - Hydromorphone
   - Hydrocodone

3. Synthetic Opioids
   - Fentanyl
   - Methadone
   - Buprenorphine
   - (Tramadol)

Opioid Outpatient Uses

- For acute pain:
  - Short acting or immediate release products

- For chronic pain (primarily cancer):
  - Agents with long half-lives
  - Long-acting or extended release formulations

- For opioid addiction:
  - Agonists (methadone)
  - Antagonists (naltrexone)
  - Partial Agonists (buprenorphine)

Opioid Effects

- Relief of physical pain
- Relief of emotional pain
- Euphoria
- Decreased anxiety; calmness
- Cough suppression
Opioid Intoxication
- Constricted pupils
- Constipation
- Nausea and vomiting (often projectile)
- Respiratory depression
- Coma and death

Opioid Withdrawal
- Dilated pupils
- Diarrhea
- Flu-like symptoms (rhinorrhea, lacrimation)
- Yawning
- Unbearable body aches
- Sweats and piloerection ("cold turkey")

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The Epidemiology of Opioid Use

Heroin Admissions: 2009

Non-Heroin Opioid Admissions: 2009

Admissions: 1999

Primary non-heroin opioid admission rates (per 100,000)
Admissions: 2001
Primary non-heroin opioid admission rates (per 100,000)

Admissions: 2003
Primary non-heroin opioid admission rates (per 100,000)

Admissions: 2005
Primary non-heroin opioid admission rates (per 100,000)

Admissions: 2007
Primary non-heroin opioid admission rates (per 100,000)

Admissions: 2009
Primary non-heroin opioid admission rates (per 100,000)

ED Visits (DAWN): 2004-2008

Admissions, Deaths, Sales: 1999-2010

The Prescription Opioids Epidemic: The Root of the Disaster

The Case of Susan

Susan is a 25-year-old construction worker who presents with moderate to severe low back pain following a failed attempt to lift a 250 lb. bag of concrete.

Thorough evaluation, including an X-ray of the region, reveals no structural abnormalities, but physical examination confirms lumbar injury.

Your next step is to recommend:

1. NSAIDs and/or acetaminophen
2. A 3-day supply of short-acting opioids
3. A 10-day supply of short-acting opioids
4. Extended-release long-acting opioids
5. Nothing—most cases resolve spontaneously
Non-Opioid Strategies
- NSAIDs and acetaminophen
- Corticosteroids
- Anticonvulsants and antidepressants
- Capsaicin for neuropathic pain
- Transdermal lidocaine
- Physical therapy
- Exercise and relaxation techniques
- Cognitive behavioral therapy

Treating Chronic Pain

The Case of John
John is a 55-year-old schoolteacher who has been suffering from chronic neck pain for approximately 2 years. Symptoms have shown exacerbations and partial remissions over the years but never resolved completely.

What is the most likely mechanism of his neck pain?
1. Neuropathic
2. Inflammatory
3. Cancer
4. Musculoskeletal
5. Compressive

1. Types of Chronic Pain
1. Nociceptive Pain:
   - Results from suprathreshold stimulation of nociceptors, which are neural receptors specialized for the detection of potentially harmful situations
   - For example, prolonged musculoskeletal injury
2. Neuropathic Pain:
   - Results from lesion or dysfunction of the sensory nervous system
   - For example, nerve compression
3. Mixed Nociceptive/Neuropathic Pain:
   - A combination of the two types of pain
     - For example, degenerative disc disease with mechanical (nociceptive) and radicular (neuropathic) pain

2. Cancer Pain
   - The goal is to provide:
     - Greatest pain relief possible, with the fewest number of side effects, and the most ease of administration
   - Opioid treatment:
     - Fixed schedule: morphine, fentanyl, oxycodone, hydromorphone
     - Breakthrough cancer pain: rapid onset opioids (ROOs)
   - Types:
     - Active
     - In partial remission
     - In complete remission

3. Depression
   1. Depression often manifests as physical pain, indistinguishable to the patient from somatic pain
   2. Assessment focuses on accompanying symptoms of:
      - Loss of pleasure
      - Loss of energy
      - Sadness
      - Appetite and sleep disturbances
      - Guilt and thoughts of death
4. Chronic Opioid Therapy for CNCP

Opioids are not first-line treatments for chronic non-cancer pain (CNCP).

Three major problems:
1. Lack of Efficacy
2. Significant Health Risks
3. Addiction

Lack of Efficacy

- Evidence of long-term efficacy for chronic non-cancer pain (>16 weeks) is limited and of low quality.
- For many patients with chronic pain, analgesic efficacy is not maintained over long time periods.

Significant Health Risks (1)

- Fractures from falls
  - Especially for patients over 60
- Hyperalgesia
- Hypogonadism and sexual dysfunction
- Chronic constipation and fecal impaction
- Chronic dry mouth and tooth decay
- Dry skin and pruritus

Significant Health Risks (2)

- Addiction
- Fatal unintentional overdose from respiratory depression
  - Especially due to the high dosage of opioid available as an ER/LA formulation
- Drug interactions
  - Especially with other CNS depressants
- Inadvertent exposure to household contacts
  - Especially children
- Drug diversion (“gifting” or selling)

Addiction

- The Myth of “Unmasking” a preexisting disease.
- The Fallacy of Positioning
  “There is very limited evidence and no one procedure or set of predictors is sufficient to clarify risk of opioid misuse or abuse.”

Opioid Treatment Guidelines

- American Pain Society and American Academy of Pain Medicine multi-disciplinary expert panel
- Chronic Opioid Therapy (COT) in Chronic Noncancer Pain (CNCP)
- 14 Areas of Concern
- 25 Recommendations
  - 21 “Low-quality evidence”
  - 4 “Moderate-quality evidence”
Specific Opioid Treatment Guidelines (1)

- Patient Selection and Risk Stratification
  - History, physical examination, testing, assessment of risk
  - Indication: moderate or severe CNCP, pain impacts function and quality of life, benefits outweigh harms
  - Benefit-to-harm evaluation (and documentation) before and on an ongoing basis during COT

- Informed Consent and Opioid Management Plans

- Initiation and Titration of COT
  - Initial treatment with opioids as a therapeutic trial
  - Individualized selection, dosing, and titration; insufficient evidence to recommend short-acting versus long-acting, or as-needed versus around the clock dosing

Chou R et al, J Pain, 2009;10(2):113-130

Specific Opioid Treatment Guidelines (2)

- Methadone
  - Cautious use by clinicians familiar with its use and risks*

- Monitoring
  - Documentation of pain intensity, level of functioning, progress toward goals adverse events, adherence to therapies, urine toxicology exams

- High-Risk Patients

- Dose Escalations, High-Dose Therapy, Opioid Rotation, Indications for Discontinuation

- Opioid-Related Adverse Effects
  - Anticipation, identification, and treatment of common opioid-associated adverse effects*

Chou R et al, J Pain, 2009;10(2):113-130

Specific Opioid Treatment Guidelines (3)

- Psychotherapeutic Co-interventions
  - Integration of psychotherapy, functional restoration, interdisciplinary therapy, adjunctive nonopioid therapies*

- Driving and Work Safety

- Medical Home and Consultation
  - Identification of a single clinician who accepts primary responsibility
  - Consultation when patients may benefit from extra skills or resources*

- Breakthrough Pain

- Opioids in Pregnancy

- Opioid Policies

Chou R et al, J Pain, 2009;10(2):113-130

5. Extended-Release Opioids

- Opioid tolerance must be demonstrated before using:
  - Any strength of ER/LA fentanyl
  - Any strength of ER/LA hydromorphone
  - ER oxycodone 60 mg or higher strength

- ER opioids have not been shown to be less addictive than short-acting opioids.

- Physical dependence can develop in days or a few weeks.

Blueprint for Prescriber Continuing Education Program,

Opioid Risk Tool

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Mark each box that applies</th>
<th>Item score if present</th>
<th>Item score if and relevant</th>
</tr>
</thead>
<tbody>
<tr>
<td>Family history of substance abuse</td>
<td>□</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>Recent history of substance abuse</td>
<td>□</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Personal history of substance abuse</td>
<td>□</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>Recent history of substance abuse</td>
<td>□</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>High risk for future addiction</td>
<td>□</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>History of psychosocial disorder</td>
<td>□</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Psychiatric disease</td>
<td>□</td>
<td>2</td>
<td>2</td>
</tr>
</tbody>
</table>

Total Score: __________ Risk Category: __________

Low Risk: 0 to 3  Medium Risk: 4 to 7  High Risk: 8 and above


Chou R et al, City Health Information, 2011.

Specifics of Extended-Release Opioids

- Tablet and capsule dosage forms must be swallowed whole. The pellets from capsule dosage forms can be sprinkled on applesauce and swallowed without chewing.

- For transdermal products, external heat, fever, and exertion can increase absorption, leading to fatal overdose.

- Transdermal products with metal foil backings are not safe for use in MRIs.

Blueprint for Prescriber Continuing Education Program,
Back to John

John has been taking 10 tablets of (5 mg hydrocodone/325 mg acetaminophen) and 2 tabs of (extended release 20 mg oxycodone each) pills daily for the past six months.

What is the most urgent medical concern?

1. Seizures
2. Respiratory Depression
3. Liver Failure
4. Renal Failure
5. Hypotensive Crisis

John

John has been taking 10 tablets of (5 mg hydrocodone/325 mg acetaminophen) and 2 tabs of (extended release 20 mg oxycodone each) pills daily for the past six months.

What is his daily Morphine Equianalgesic Dose (MED)?

1. (50+40) = 90
2. (50+60) = 110
3. (100+80) = 180
4. (100+120) = 220
5. I have no idea. You totally lost me here …

Calculating MED for John

10 x 5 mg hydrocodone = 50 MED (5 HC: 5 MS)
2 x 20 mg oxycodone = 60 MED (20 Oxy: 30 MS)

Therefore: MED = 50 + 60 = 110

Reassess for MED over 100!

6. Acetaminophen Warning

Hepatotoxicity can result from prolonged use of combination opioid/acetaminophen products.

- Short-term use (<10 days) – 4,000 mg/day
- Long-term use – 2,500 mg/day


7. Morphine (Oral) Equianalgesic Doses

1. Naturally Occurring Opioids
   - Morphine 30
   - Codeine 200

2. Semi-Synthetic Opioids
   - Oxymorphone 10
   - Oxycodone 20
   - Hydromorphone 7.5
   - Hydrocodone 30

8. Discontinuation

Tapering the opioid dose is necessary to safely discontinue treatment with Extended Release or Long Acting opioids when therapy is no longer needed.

Protocols
- 10% every day
- 20% every 3-5 days
- 25% every week

9. Ongoing Management

- Establish goals for therapy and continuously evaluate pain as well as functioning level and quality of life.
- Parts of a Patient Provider Agreement (PPA):
  - Participants
  - Information (physical dependence, addiction)
  - Expectations (Urine Toxicology Exams, permissions)
  - Prescriptions (scheduled appointments, on-call)
  - Reasons for ending the agreement
  - Attestation


Urine Toxicology False Positives

Use of which one of the following can turn a Urine Toxicology Examination positive for both codeine and morphine?

1. Heroin
2. Hydrocodone
3. Oxycodeone
4. Poppy seed bagels
5. All of the above

10. Urine Toxicology Interpretation


Urine Toxicology Detection Limits

- Alcohol 7-12 hours
- Alcohol (Ethyl glucuronide, EtG test) 4 days
- Amphetamines/Methamphetamines 2 days
- Benzodiazepines (Short-acting) 3 days
- Benzodiazepines (Long-acting) 30 days
- Cocaine 2-4 days
- Heroin (Morphine) 2 days
- Methadone 3 days
- Marijuana (Single use) 3 days
- Marijuana (Long-term heavy use) >30 days


And one more … Advice for John

John has decided to undertake an opioid discontinuation trial. He asks for specific advice while he is still taking opioids.

All of the following are good recommendations, EXCEPT:

1. Fill your prescriptions at one pharmacy
2. Keep medications in a secure location, preferably locked.
3. Avoid alcohol, benzodiazepines, muscle relaxants, and monoamine oxidase inhibitors (MAOIs)
4. Discard unused medication down the toilet
5. All of the above are excellent recommendations!

Addiction
The Case of Helen

Helen is a 35-year-old ophthalmologist who has been addicted to prescription opioids since she was a sophomore in college. Her wife, Linda, just found out about it and brings Helen to you for advice.

What is the first line treatment of opioid dependence?

1. Oral Naltrexone
2. Injectable Naltrexone
3. Buprenorphine/Naloxone
4. Buprenorphine
5. Motivational Enhancement Therapy and Cognitive Behavioral Therapy
Treatment of Opioid Dependence:
Two Main Strategies

1. Agonists
   - Nicotine Replacement Therapies
   - Methadone for Opioids

2. Antagonists
   - Naltrexone for Opioids

Renner and Levounis, Office-Based Buprenorphine Treatment of Opioid Dependence, 2011.

The New Strategy

Partial Agonists
   - Varenicline for Nicotine
   - Buprenorphine for Opioids

Renner and Levounis, Office-Based Buprenorphine Treatment of Opioid Dependence, 2011.

The Ceiling Effect

![Graph showing the ceiling effect of full agonists (Methadone), partial agonists (Buprenorphine), and antagonists (Naloxone).]

Renner and Levounis, Office-Based Buprenorphine Treatment of Opioid Dependence, 2011.

Back to Helen

Helen and Linda are planning to have a baby in 2013.

If Helen is going to be the biological mother, what should they know about the risk of neonatal abstinence syndrome?

1. It is more severe if the mother is treated with methadone rather than buprenorphine.
2. It is more severe if the mother is treated with buprenorphine rather than methadone.
3. There are no reliable data to inform the parents one way or the other.


Neonatal Abstinence Syndrome

![Graph showing mean total hours of dependency and mean hospital stay (days) for different treatments.]


6

Conclusions
Take Home Messages

- Prescription opioid use has now become a nationwide epidemic
- Acute pain can be successfully treated with a limited course of short-acting opioids
- Opioids have been shown to be neither very effective nor very safe in the treatment of chronic non-cancer pain
- Management of patients on chronic opioid therapy should include a written agreement and ongoing patient monitoring to ensure adherence to the treatment plan
- Buprenorphine is the first-line treatment for opioid addiction

Q1. Post-Activity Audience Response Question

Long-term efficacy of opioids for chronic non-cancer pain has been well established.

1. True
2. False
3. Not sure

Q2. Post-Activity Audience Response Question

Patient risk factors for opioid abuse include:

1. Age > 45 years
2. History of childhood obesity
3. History of depression
4. All of the above

Q3. Post-Activity Audience Response Question

Which of the following is TRUE regarding extended-release/long-acting (ER/LA) opioids?

1. A patient should not start on a ER/LA opioid regimen if already opioid tolerant
2. Overdose from transdermal preparations can occur if the patient becomes febrile
3. ER/LA opioids are less addictive than short-acting opioids
4. All of the above

Thank you