Addressing the Opioid Epidemic: The Art & Science of Opioid Tapering
July 11, 2018
Five Pillars

- **Education**
- **Take Back Program**
- **Law Enforcement**
- **Prescription Drug Monitoring Program**
- **Treatment**
Objectives

• Recognize appropriate opioid tapering practices
• Identify patient characteristics that may affect opioid tapering
• Understand withdrawal symptoms and management
Today’s Speaker

Eric Christianson, PharmD, BCGP, BCPS
Clinical Pharmacist
www.meded101.com
THE ART AND SCIENCE OF OPIOID TAPERING

Eric Christianson PharmD, BCGP, BCPS
Consultant Pharmacist
Meded101.com
DISCLOSURE/CONFLICTS OF INTEREST

• No conflicts of interest related to the material presented
OBJECTIVES

• Recognize appropriate opioid tapering practices
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• Understanding withdrawal symptoms and management
TERMINOLOGY

• Morphine milligram equivalent (MME)
• Morphine equivalent dose (MED)
TOLERANCE

• Drug tolerance is a pharmacology concept where a patient’s reaction to a specific drug and concentration of the drug is reduced followed repeated use, requiring an increase in concentration to achieve the desired effect

• Patient’s need more and more drug to get the same effect

• Declines when patients abstain
ADDICTION

• Chronic, relapsing brain disease that is characterized by compulsive drug seeking and use, despite harmful consequences. It is considered a brain disease because drugs change the brain; they change its structure and how it works.
Substance dependence also known as drug dependence is an adaptive state that develops from repeated drug administration, and which results in withdrawal upon cessation of drug use.

Withdrawal symptoms can be awful for patients and be a significant factor for addiction.
OPIOID DEPENDENCE VS. OPIOID ADDICTION

Opioid Dependence is defined as an increase in need of opioid dosage to obtain optimum pain relief. Opioid addiction results in increased consumption of opioids to maintain euphoric and erratic mood.

Source: ePainAssist.com
<table>
<thead>
<tr>
<th>Medication</th>
<th>Equianalgesic doses</th>
<th>Route of Admin</th>
<th>Half-life (hours)</th>
<th>Duration of analgesic effect (hours)</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fentanyl patch</td>
<td>12.5 mcg/hr</td>
<td>Transdermal</td>
<td></td>
<td>48-72**</td>
<td></td>
</tr>
<tr>
<td>Levorphanol</td>
<td>4 mg</td>
<td>Oral</td>
<td>11-16</td>
<td>4-8</td>
<td></td>
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<tr>
<td>Hydromorphone</td>
<td>7.5 mg</td>
<td>Oral</td>
<td>2-3</td>
<td>3-6</td>
<td>IR, SR or ER forms have same equianalgesic potency</td>
</tr>
<tr>
<td>Oxymorphone</td>
<td>15 mg</td>
<td>Oral</td>
<td>7-9</td>
<td>4-6</td>
<td>IR and ER forms have same equianalgesic potency</td>
</tr>
<tr>
<td>Oxycodone</td>
<td>20 mg</td>
<td>Oral</td>
<td>2-3</td>
<td>3-6</td>
<td>IR and SR forms have same equianalgesic potency</td>
</tr>
<tr>
<td>Morphine</td>
<td>30 mg</td>
<td>Oral</td>
<td>2-3</td>
<td>3-6</td>
<td>IR, SR or ER forms have same equianalgesic potency</td>
</tr>
<tr>
<td>Hydrocodone</td>
<td>30 mg</td>
<td>Oral</td>
<td>3-4</td>
<td>4-8</td>
<td></td>
</tr>
<tr>
<td>Tramadol (IR)</td>
<td>150mg</td>
<td>Oral</td>
<td>6-9</td>
<td>3-11</td>
<td></td>
</tr>
<tr>
<td>Codeine</td>
<td>200 mg</td>
<td>Oral</td>
<td>2-4</td>
<td>4-6</td>
<td></td>
</tr>
<tr>
<td>Meperidine</td>
<td>300mg</td>
<td>Oral</td>
<td>2.5-4</td>
<td>2-4</td>
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</tr>
</tbody>
</table>
GENETICS IN CONVERSION

• Oxycodone
  • CYP3A4, 2D6
• Morphine
  • Hepatic Conjugation
• Codeine (prodrug)
  • CYP2D6
• Fentanyl
  • CYP3A4
RISKS ASSOCIATED WITH OPIOIDS

- Constipation
- Respiratory Depression
- Sleep-disordered breathing
- Fractures
- Hypothalamic-pituitary-adrenal suppression
  - Lower testosterone levels
- Overdose
- Hyperalgesia
CLINICAL CONTROVERSY

- Hyperalgesia
  - Heightened sensitivity to pain
  - First discovered in rats
- Factors that may increase risk
  - Aggressive titration/escalation
  - Length of use
  - Chronic pain management on higher doses
2017 CANADIAN GUIDELINES FOR OPIOID TAPERING IN CHRONIC PAIN

- Gradually reduce 5% to 10% of the morphine-equivalent dose every 2 to 4 weeks with frequent follow-up
- Switch the patient from immediate-release to extended-release opioids on a fixed dosing schedule
- Collaborate with a pharmacist to assist with scheduling dose reductions
- There is limited evidence available to guide the design of tapering regimens. General information is provided in the Guideline
| Slowest Taper  
  (over years) | Slower Taper  
  (over months or years) | Faster Taper  
  (over weeks)*** | Rapid Taper  
  (over days)*** |
<table>
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<tr>
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</thead>
<tbody>
<tr>
<td>Reduce by 2 to 10% every 4 to 8 weeks with pauses in taper as needed</td>
<td>Reduce by 5 to 20% every 4 weeks with pauses in taper as needed</td>
<td>Reduce by 10 to 20% every week</td>
<td>Reduce by 20 to 50% of first dose if needed, then reduce by 10 to 20% every day</td>
</tr>
<tr>
<td>Consider for patients taking high doses of long-acting opioids for many years</td>
<td>MOST COMMON TAPER</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Month 1:</td>
<td>90 mg SR qam, 75 mg noon, 90 mg qpm [5% reduction]</td>
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<td></td>
</tr>
<tr>
<td>----------</td>
<td>-------------------------------------------------</td>
<td></td>
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<tr>
<td>Month 2:</td>
<td>75 mg SR qam, 75 mg noon, 90 mg qpm</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Month 3:</td>
<td>75 mg SR (60 mg+15 mg) Q8h</td>
<td></td>
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<tr>
<td>Month 4:</td>
<td>75 mg SR qam, 60 mg noon, 75 mg qpm</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Month 5:</td>
<td>60 mg SR qam, 60 mg noon, 75 mg qpm</td>
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<tr>
<td>Month 6:</td>
<td>60 mg SR Q8h</td>
<td></td>
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<tr>
<td>Month 7:</td>
<td>60 mg SR Q8h</td>
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<tr>
<td>Month 8:</td>
<td>30 mg SR Q8h</td>
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<tr>
<td>Month 9:</td>
<td>15 mg SR Q8h</td>
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</tr>
</tbody>
</table>

Ex: morphine SR 90 mg Q8h = 270 MEDD

<table>
<thead>
<tr>
<th>Week 1:</th>
<th>75 mg SR Q8h [16% reduction]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Week 2:</td>
<td>60 mg SR (15 mg x 4) Q8h</td>
</tr>
<tr>
<td>Week 3:</td>
<td>45 mg SR (15 mg x 3) Q8h</td>
</tr>
<tr>
<td>Week 4:</td>
<td>30 mg SR (15 mg x 2) Q8h</td>
</tr>
<tr>
<td>Week 5:</td>
<td>15 mg SR Q8h</td>
</tr>
<tr>
<td>Week 6:</td>
<td>15 mg SR Q12h</td>
</tr>
<tr>
<td>Week 7:</td>
<td>15 mg SR QHS x 7 days, then stop***</td>
</tr>
</tbody>
</table>

Ex: morphine SR 90 mg Q8h = 270 MEDD

<table>
<thead>
<tr>
<th>Day 1:</th>
<th>60 mg SR (15 mg x 4) Q8h [33% reduction]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Day 2:</td>
<td>45 mg SR (15 mg x 3) Q8h</td>
</tr>
<tr>
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<tr>
<td>Days 5-7:</td>
<td>15 mg SR Q12h</td>
</tr>
<tr>
<td>Days 8-11:</td>
<td>15 mg SR QHS, then stop***</td>
</tr>
</tbody>
</table>
ABERRANT BEHAVIORS

• According to guidelines from the American Pain Society and the American Academy of Pain Medicine, patients "who engage in repeated aberrant drug-related behaviors or drug abuse/diversion, experience no progress toward meeting therapeutic goals, or experience intolerable adverse effects" should be tapered or weaned off chronic opioid therapy.
TAPERING CONSIDERATIONS

• Appropriate patient
  • Stability
    • Mental health concerns
    • Pain/Surgery
  • Do they have the desire?
    • Motivational interviewing
MOTIVATIONAL INTERVIEWING

• Listen/Empathy
• Non-confrontational
• Try to focus on positive
• Avoid directions/orders
  • Encourage them to devise plan and/or give options in process
• Let them explore what will be difficult, but also what might be beneficial
OPIOID USE CONSIDERATIONS

• Length of use
• Current dose
• Patient Expectations
• Tapering
PATIENT MANAGEMENT

• Goals
  • Short term
  • Long term
• Withdrawal
• Setting expectations
  • Realistic
• Managing setbacks
WITHDRAWAL SYMPTOMS

• Dilated pupils
• Tachycardia
• Goose bumps
• Tachypnea
• Hypertension
• Nausea
• Body aches

• Diaphoresis
• Tremor
• Rhinorrhea
• Abdominal cramps, Diarrhea
• Insomnia
• Anxiety
• ***non-life threatening
WITHDRAWAL MANAGEMENT

- Withdrawal minimization with slow taper
- Non-pharmacologic interventions
  - Nausea
  - Sleep hygiene
  - Coping techniques
  - Pain
WITHDRAWAL MANAGEMENT

**Pharmacologic**

- Clonidine 0.1 mg PO two to three times daily as needed for hypertension, nausea, cramps, diaphoresis, tachycardia
- Trazodone 25 - 50 mg PO at bedtime as needed for insomnia
- Diphenhydramine 25 - 50 mg PO every four hours as needed for insomnia, restlessness
- Ibuprofen 200 - 400 mg PO every eight hours as needed for muscle aches
- Acetaminophen 500 – 1,000 mg PO every six hours as needed for muscle aches; do not exceed 4,000 mg / 24 hours
- Loperamide 2 mg PO after each loose stool; do not exceed 16 mg/day
ALTERNATIVE WITHDRAWAL AGENTS

• Baclofen
• Gabapentin
• Bismuth Subsalicylate
• Hydroxyzine
• Anti-nausea meds
• Avoid Benzodiazepines
ADJUNCT ANALGESICS

- Anticonvulsants
  - i.e. gabapentin, pregabalin
- TCA’s
- SNRI’s
- Simple analgesics
  - NSAIDs or acetaminophen
- Topicals
- Non-pharmacologic therapies
TAPERING DOWN

• Remembering the goal
  • MED target
  • Taper off

• Rate
  • Patient factors (withdrawal, length of use, work/life schedule etc.)
  • 3 days, weekly, every other week, monthly
  • Typical start approximately 10% reduction
TIMELINE

- Patient specific
  - Starting Dose
  - Goals
- Typical taper will take several weeks and many will require months or possibly years
- Patience and flexibility!
MEDICATION FACTORS

- Dosage forms!
- Kinetics
  - i.e. long acting versus short acting
  - Methadone
TOLERANCE

- Tolerance for a given dose disappears in approximately 1-2 weeks
- Risk for overdose
- Educate patients about this
  - Very important for patients who have been on higher doses
TIPS

- Last 20-60 MED may be challenging (slow down)
  - Immediate release preparations may be helpful here (split tabs)
  - Extending dosing interval
- Avoid Benzo’s for withdrawal symptoms
- Monitoring PMP
- Don’t reincrease opioid dose
  - Hold taper for patient instability
DISCONTINUATION STRATEGIES

- Having short acting available
  - Split doses
- Extending dosing interval
- ***Continued education about tolerance
CASE #1

- 64 year old male
- Numerous back surgeries/MVA
- Pain 7/10
- Escalating doses over the last 5 years
  - Morphine ER 60mg BID
  - Oxycodone 5mg four times per day
- Tried on numerous antispasmodics w/o benefit
  - Baclofen
  - Cyclobenzaprine
  - Soma
CASE #1

• PCP concerned with escalating doses and non-response, would like to at least taper to 90 MED (60 mg oxycodone)

• Patient in agreement given recent news about opioid epidemic
CASE #1

• Questions to consider:
  • Patient receptiveness?
    • Has he been educated about risks?
  • Pain augmenting agents not yet tried
  • Tried off in the past?
  • Missed/late doses, what happened?
  • Tried reduced doses?
  • Withdrawal symptoms?
CASE #1

- Target 5-20% reduction
- I typically target 10% initially unless patient is highly motivated
- Total morphine equivalent 150 mg/day
  - Morphine ER 60 mg BID
  - Oxycodone 5 mg four times per day
- Ask patient preference
  - Could do 10 mg of oxycodone
  - Could do 15 mg of morphine
CASE #2

- 45 y/o female
- Failed urine drug screen, provider concerned and desires taper if going to continue to provide care (positive for other opioids and marijuana which were not declared by patient)
- Patient agrees to begin taper process (reluctantly)
- Chronic abdominal pain
- Chronic back pain for previous injury of falling off a ladder years ago
- Anxiety and Panic disorder, followed by behavioral health
- History of cirrhosis with ascites
  - Fluid/pressure is painful for her
  - Seeing GI specialist
CASE #2

- Lisinopril 5 mg BID
- Oxycodone CR 30 mg BID
- Furosemide 40 mg once daily
- Gabapentin 600 mg TID
- Cyclobenzaprine 10 mg HS
- Thiamine 100 mg once daily
- Naproxen 440 mg BID
- Calcium/D 600 mg once daily
- Bupropion 300 mg once daily
- Spironolactone 100 mg once daily
- Ambien 10 mg at bedtime as needed

- Zaditor 1 gtt both eyes BID prn
- Lidocaine patches 1 patch to AA PRN
- Diazepam 10 mg four times per day
- Duloxetine 60 mg once daily
- Oxycodone 15 mg six times per day
- Vitamin D 2000 units per day
- Rifaximin 550 mg BID
- Folic acid 1 mg once daily
- Simethicone 80 mg four times per day
CASE #2

• Initial Step – 15 mg reduction in immediate release oxycodone (15 mg five times per day)

• Substantial sweating, diarrhea, stomach upset, insomnia, and muscle twitching reported at 1 and 2 week telephone follow up

• Pain increased with reduction (initial = 7, following decrease 8-9) – primarily GI pain

• Clonidine prescribed as needed with monitoring of BP for hypotension (historically in 120-140 range systolic)
CASE #2

- 4 week check-in
- Clonidine mildly helpful
- Pain was down to 7/10 (original pain level)
- Felt as if she was thinking a little more clearly (did start Bupropion per psych as well)
- Patient reluctant to reduce again, but willing to try to reduce by 5 mg this time
- Struggling with insomnia (Ambien which had been effective in past, not helping)
  - Trial trazodone in its place
CASE #2

- 2 week telephone follow up (week 6)
- Will not reduce further at this time
- Significant diarrhea – attributed to withdrawal
  - Wants something to help with this
  - Loperamide Rx as needed
CASE #2

- 4 week follow up (week 8)
- Current dose of oxycodone immediate release 15 mg four times per day and 10 mg once per day
- Willing to try off 10 mg dose after discussion
CASE #2

• 2 Week telephone follow-up (week 10)
• Substantial diarrhea right after reduction
  • Improving now
  • After initial increase, seems to be back to baseline
• Will not consider decrease at this time
• Patient does not want to reduce by 10 mg or more again
CASE #2

• 4 week follow up (Week 12)
• Current dose oxycodone 15 mg four times per day
• Uses clonidine and loperamide after reduction; trazodone not effective, has restarted using zolpidem as Rx’d by psych before
• Will only reduce by 5 mg
• Reduced dose at 15 mg three times per day and 10 mg once per day
CASE #2

• Hx of illicit drug use
• Hospitalized for overdose
• Entered into treatment program for addiction
CASE #3

- 65 y/o female
- DDD
- Fibromyalgia
- Morbid Obesity (wheelchair bound)
- Diabetes
- CHF
- Dry Eye
- Emphysema
- Depression
- HTN
- Afib
CASE #3

- Potassium 20 meq once daily
- Tramadol 100 mg q12 hr PRN
- Metolazone 2.5 mg twice/week
- Warfarin
- Gabapentin 300 mg TID
- Duloxetine 30 mg once daily
- Ferrous Sulfate 325 once daily
- Trazodone 50 mg HS
- Pulmicort neb 0.5 mg BID
- Duonebs four times per day
- Miralax as needed
- Fentanyl 75 mcg q3 days
- Pravastatin 20 mg once daily
- Prozac 40 mg once daily
- Wellbutrin XL 150 mg once daily
- Protonix 40 mg daily
- Humalog 30 units TID
- Toujeo 96 units once daily
- Spironolactone 25 mg daily
- Acetaminophen 1,000 mg as needed
- Senna-S 2 tablets as needed
CASE #3

- Patient has seen negative press on TV on Fentanyl – motivated to taper
- Has been on lower doses in the past
- Would like to be more aggressive
- Reduction from 75 mcg to 50
- Planned follow up at 2 weeks by phone and 4 weeks to possibly reduce again
- Very rare use of tramadol or acetaminophen (no hx of liver concerns)
  - Encouraged use of acetaminophen first
  - Avoid Ibuprofen/NSAIDs - warfarin
Follow up at 2 weeks

Taking a little acetaminophen for back aches and pains

No tramadol use

Stomach upset – no vomiting
  - Using Pepto-Bismol and Tums as needed
  - Encouraged avoidance of Pepto-Bismol given concerns with warfarin
CASE #3

- 4 Week Follow Up
- Doing well, hasn’t notice much of an increase in pain
- Desire to reduce to 25 mcg patch which she has done before
- Mild stomach upset continues, but improved compared to 2 week mark
- Planned follow up in 4 weeks
CASE #3

• Week 8 – Recent urinary tract infection that is painful
  • 2 days on antibiotic at this point
• Taking tramadol as needed 50 mg 1-2 times per day
• Planned follow up in 1 week to reassess taper – kept at 25 mcg patch for another 7-10 days

• Week 9;
  • Mild GI upset, but only doing Rolaids 1-2 times per day
  • plan reduction to 12 mcg patch
CASE #3

- Week 13
- Discontinued fentanyl patch
- Continued mild stomach upset following discontinuation
- Tolerable discontinuation without much tramadol use
REFERENCES


• http://www.agencymeddirectors.wa.gov/Calculator/DoseCalculator.htm

• Maria Soledad Cepeda, Vivienne Zhu, Gary Vorsanger, Gary Eichenbaum; Effect of Opioids on Testosterone Levels: Cross-Sectional Study using NHANES, Pain Medicine, Volume 16, Issue 12, 1 December 2015, Pages 2235–2242, https://doi.org/10.1111/pme.12843

Questions
Medication Safety LAN
Upcoming Events

• The Opiate ‘Crisis’: Physician Perspective and Opiate Stewardship – August 7 – 12-1pm CT

• Medication Assisted Treatment of Opioid Use Disorder – September 26, 12-1pm CT
  – Registration information coming!
Wrap Up

• Resources
  – CDC Guideline for Prescribing Opioids for Chronic Pain
    • https://www.cdc.gov/drugoverdose/prescribing/guideline.html
  – CDC Training for Providers
    • https://www.cdc.gov/drugoverdose/training/index.html
  – CDC Clinical Tools
    • https://www.cdc.gov/drugoverdose/prescribing/clinical-tools.html
Contact Information

Beth Nech, MA
Project Manager
bnech@kfmc.org
Kansas Foundation for Medical Care
800 SW Jackson St, Ste 700
Topeka, KS 66612
P: 785.271.4120

Paula Sitzman, RN, BSN
Quality Improvement Advisor
paula.sitzman@area-a.hcqis.org
CIMRO of Nebraska
1200 Libra Drive, Suite 102
Lincoln, Nebraska 68512
P: 402.476.1399, Ext. 512

Sally May, RN, BSN, CH-GCN
Senior Quality Improvement Specialist
sally.may@area-a.hcqis.org
Jayme Steig, , PharmD, RPh
Quality Improvement Program Manager
jayme.steig@area-a.hcqis.org
Quality Health Associates of North Dakota
41 36th Ave NW
Minot, ND 58703
P: 701.989.6220

Linda Penisten, RN, OTR/L
Program Manager
linda.penisten@area-a.hcqis.org
South Dakota Foundation for Medical Care
2600 West 49th Street, Suite 300
Sioux Falls, SD 57105
P: 605-444-4124

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