

Opioid Discontinuation: The Art of Tapering

Julie Cunningham, Pharm D, BCPP
Department of Pharmacy
Mayo Medical Center, Rochester, MN
Assistant Professor of Pharmacy
College of Medicine Mayo Clinic

Objectives:

- Discuss current literature evidence for safe tapering of opioids in patients with chronic use.
- Review opioid withdrawal symptoms and factors that may contribute to the intensity of symptoms.
- Describe relevant pharmacokinetic information that impacts the development of opioid tapers.
- Discuss concurrent medications, disease states that may require opioid taper adjustments.
- Review case examples and develop plans to taper opioids.



Current Evidence for Opioid discontinuation

- Why discontinue opioid use?
 - No longer needed
 - Opioid use is chronic non-cancer pain (CNCP) is controversial
 - Hyperalgesia
 - Patient/Prescriber dissatisfaction
 - Abuse

Ahmed et al. Amer J of Hosp Pall Med.2010;27
Rome et al. Mayo Clinic Proc.2004;79
Chu et al. J Pain 2006;7
Miller et al. Amer J Ther 2006;13

Current Literature for Opioid Withdrawal:

- Limited to literature describing the use of methadone and buprenorphine as replacement
- Adjuvants:
 - Anticonvulsants
 - Buspirone
 - Antidepressants

Kheirabadi et al. Addiction.2008;103
Buydens-Branchey et al. J Clin Psychopharmacol.2005;25
Lin et al. J Clin Psychopharmacol. 2008; 28

CNCP opioid withdrawal in a pain rehabilitation setting:

- 3 week multidisciplinary pain rehabilitation program
- Primary goal of functional improvement
 - 99 patients on daily opioids
 - Mean dose 78.4 mg oral morphine equivalence (MOE)
 - Significant reduction in pain severity at the end of the 3 weeks with opioid discontinuation ($p < .001$)

Rome et al. Mayo Clinic Proc.2004;79

CNCP opioid withdrawal in a pain rehabilitation setting:

- Longitudinal experience 6 month following program completion (n=238/340 program completers):
 - 10.7% of opioid users were taking for 10 or more years
 - Mean MOE dose was 99 mg
 - Patients on both low and high (< and >100 mg/day) continued to have significant improvements in pain severity (p<.001)
 - 13.9% of patient taking opioids at 6 month follow-up
 - Majority taking at time of admission
 - Mean MOE dose was 67.6 mg

Townsend et al. Pain. 2008;140

Opioid withdrawal in an Addiction detoxification program:

- Retrospective sample of prescription opioid medication detoxification in an inpatient addiction treatment unit (n=53):
 - Abrupt opioid med DC on admission
 - Detoxification ave of 5 days
 - 64% hydrocodone, 23% oxycodone ER
 - Mean dose = 16.8 dosage forms/day
 - Ave use 3.7 years
 - Diazepam and clonidine adjuvant agents during detoxification
 - Self-reported pain scores; Admit = 5.5; DC = 3.4

Miller et al. Amer J Ther 2006;13

How do I get there??



Opioid Detoxification Regimens:

- Katrina Disaster Working Group; AAPM,2005
 - Reduction of daily dose by 10% each day, or
 - Reduction of daily dose by 20% every 3-5 days, or
 - Reduction of daily dose by 25% each week

Opioid Detoxification Regimens:

- US Veterans Affairs Administration (USVA); 2010
 - Slow: Reduce 20-50% per week of original dose
 - Rapid:
 - **Methadone:**
 - Decrease dose by 20-50% per day until you reach 30 mg/day,
 - Then decrease by 5 mg/day every 3-5 days to 10 mg/day,
 - Then decrease by 2.5 mg/day every 3-5 days.

2010 VA/DoD Clinical Practice Guideline
Management of Opioid Therapy for Chronic Pain

Opioid Detoxification Regimens:

- US Veterans Affairs Administration (USVA); 2010
 - Rapid:
 - **Morphine SR/CR:**
 - Decrease dose by 20-50%per day until you reach 45 mg/day,
 - Then decrease by 15 mg/day every 2-5 days.
 - **Oxycodone CR: (IR use similar schedule)**
 - Decrease dose by 20-50% per day until you reach 30 mg/day,
 - Then decrease by 10 mg/day every 2-5 days.

2010 VA/DoD Clinical Practice Guideline
Management of Opioid Therapy for Chronic Pain

Educate on Withdrawal Symptoms, Taper Medications

- Taper schedule should be made on an individual basis
 - How acute is the need to taper?
 - Duration of Use
 - Anxiety related to tapering
 - Psychosocial factors:
 - Tapering difficulties is associated with:
 - Multiple co morbidities
 - Polysubstance abuse
 - Female gender
 - Older age

Kral. Pain Treatment Topics. 2006

Clinical Opioid Withdrawal Scale (COWS): -11 item clinician administered

- Pulse
- Sweating
- Restlessness
- Pupil size
- Bone or Joint aches
- Runny nose, tearing
- GI upset
- Tremor
- Yawning
- Anxiety Irritability
- Gooseflesh skin

Score: 5-12 mild; 13-24 moderate; 25-36 moderately severe; >36 severe

Wesson et al. J Psychoactive Drugs 2003;35; Tompkins et al. Drug Alcohol Dep 2009; 105

Opioid Withdrawal Factors

- Total Daily Dose
- Determine Morphine equivalent dose
 - Multiple published tables
 - Electronic programs
- Short-acting or Long-acting opioid
- Patient past experience of withdrawal from opioids

Opioid Withdrawal Adjuvant Therapy:

- Clonidine:
 - Autonomic symptoms (HTN, nausea, cramps, diaphoresis, tachycardia)
 - Various protocols have used oral or transdermal patches
- Antihistamines/Trazodone
 - Insomnia
- NSAIDs
 - Muscle aches
- Loperamide
 - Diarrhea

Opioid Tapering general principles from the CNCP perspective:

- Stabilize daily dose
 - If patient takes as needed, determine average dose
- Consider oral morphine daily equivalent dose
- Consider product formulation restrictions
 - Half-tabs, quarter tabs
 - Smallest strength of extended release products




Hydrocodone

- Most frequently prescribed prescription medication 2010 (Forbes.com)
- Available as combination product with acetaminophen or ibuprofen
 - High number of tablets may necessitate rapid detoxification or conversion to a different opioid for tapering
- FDA change (1/13/11):
 - The U.S. Food and Drug Administration is asking manufacturers of prescription combination products that contain acetaminophen to limit the amount of acetaminophen to no more than 325 milligrams (mg) in each tablet or capsule.
 - Phased in over 3 years.

Hydrocodone Pharmacology:

- Half-life: 4 hours
- Duration: 4-6 hours
- Peak: 1.3 hours
- Morphine Oral equivalence = 1:1
- Hydrocodone/acetaminophen
 - 2.5, 5, 7.5, and 10/500; 7.7 and 10/650; 10/660; multiple strengths of elixirs and solutions
- Hydrocodone/ibuprofen:
 - 7.5/200mg



Hydrocodone Case:

- LB is a 46 yof with Fibromyalgia. She has been on Hydrocodone/APAP 10/500 mg 2 tablets every four times daily for 2 years (MOE = 80 mg). PMH: Hyperlipidemia, Depression
- Vitals on admission: BP 126/82; HR 76
- Other medications: NSAID, muscle relaxant, allergy meds, simvastatin, venlafaxine, zolpidem
- Taper Plans: reduce by 10 mg per day, until 40 mg/ day then reduce by 1/2 tab per day; hold dose on weekends;
- Total taper = 17 days


Hydrocodone Taper:

| Day | 0600 | 1400 | 1800 | 2200 | Total dose | BP | HR | COWS score |
|-------|------|------|------|------|------------|--------|-----|------------|
| Thurs | 20 | 20 | 10 | 20 | 70 | | | |
| F/S/S | 20 | 10 | 10 | 20 | 60 | 128/73 | 101 | 4 |
| Mon | 10 | 10 | 10 | 20 | 50 | 116/77 | 81 | 2 |
| Tues | 10 | 10 | 10 | 10 | 40 | 122/85 | 107 | 6 |
| Wed | 10 | 10 | 5 | 10 | 35 | 124/70 | 96 | 4 |
| Thurs | 10 | 5 | 5 | 10 | 30 | | | |
| Fri | 5 | 5 | 5 | 10 | 25 | 119/73 | 112 | 9 |
| S/S | 5 | 5 | 5 | 5 | 20 | | | |
| Mon | 5 | 5 | - | 5 | 15 | 135/83 | 102 | 4 |
| Tues | - | 5 | - | 5 | 10 | 110/66 | 93 | 4 |
| Wed | - | - | 5 | - | 5 | 127/83 | 107 | 4 |

Oxycodone Pharmacology:

- Half-life: IR = 3.5-4hr; ER = 4.5-8hrs
- Morphine Oral equivalence = 1:1.5
- Oxycodone immediate release:
 - 5 mg capsules, 5, 10,15, 20, 30 mg tablets
 - 20mg/ml oral solution
- Extended release:
 - 10, 15, 20, 30, 40, 60 and 80mg tablets (15 mg only brand name product)

Oxycodone Case:



- AC is a 72 yof with low back pain x10 years. She has been on oxycodone ER 40 mg twice daily and oxycodone IR 5 mg tid for the past 8 months (MOE = 143 mg).
- PMH: HTN, osteoporosis, hyperlipidemia, COPD, GERD
- Vitals on admission: BP 124/67; HR 46
- Other medications: Duloxetine, clonazepam, diltiazem, metoprolol, HCTZ, HRT
 - Taper Plans: Hold Oxycodone IR at current dose. Reduce oxycodone ER by 10 mg per day; hold dose on weekends; Following completion of oxycodone ER, taper oxycodone IR by 2.5 mg daily.
 - Total taper = 15 days

Oxycodone ER Taper:

| Day | 0800 | 2000 | Total dose | BP | HR | COWS score |
|---------|--------|------|------------|--------|----|------------|
| Wed | 30 | 40 | 70 | 125/58 | 50 | 0 |
| Thur | 30 | 30 | 60 | | | |
| F/S/S/M | 20 | 30 | 50 | 112/65 | 49 | 2 |
| Tues | 20 | 20 | 40 | | | |
| Wed | 10 | 20 | 30 | 124/70 | 52 | 2 |
| Thurs | 10 | 10 | 20 | 130/72 | 54 | 2 |
| F/S/S | | 10 | 10 | | | |
| M/Tues | 5 (IR) | 5 | 10 | | | |
| Mon | 2.5 | 5 | 7.5 | 150/75 | 52 | 8 |
| Tues | 2.5 | 2.5 | 5 | 137/72 | 84 | 5 |
| Wed | - | 2.5 | 2.5 | 150/87 | 90 | 8 |

Pt complaints of dizziness; metoprolol dose decreased

Metoprolol dose resumed

Fentanyl Patches:

- MOE: 1:100
- Patches: 12, 25, 50,75, 100 mcg strengths; deliver the amount per hour
 - 12 mcg patch contains 2100 mcg fentanyl
 - 25 mcg patch contains 4200 mcg fentanyl
 - 50 mcg patch contains 8400 mcg fentanyl
 - 75 mcg patch contains 12,600 mcg fentanyl
 - 100 mcg patch contains 16,800 mcg fentanyl

Fentanyl TD Patch differences:

- Reservoir membrane-modulated systems:
 - *The drug is contained in a reservoir between an impermeable backing layer and a rate-controlling microporous membrane. Drug release is controlled by the membrane. Cutting the patch makes the entire dose available immediately.*
- Matrix systems:
 - *The drug is evenly distributed throughout a drug-in-adhesive matrix similar to that of the drug-in-adhesive layer system. Again, the amount of available drug is directly proportional to the surface area of the patch. Cutting the patch is generally possible but may decrease the efficacy of the adhesive.*
- Recommended not to cut any type of fentanyl patch.

ISMP, 2008:13

Fentanyl patches

- Discontinuation:
 - Upon system removal, 17 hours or more are required for a 50% decrease in serum fentanyl concentrations (Duragesic® PI)
 - Serum fentanyl concentrations increase gradually following initial application, generally leveling off between 12 and 24 hours and remaining relatively constant, with some fluctuation, for the remainder of the 72-hour application period



Fentanyl Patch case:

- AC is a 37 yof with abdominal and joint pain x14 years. She has been on Fentanyl patches 200 mcg changed every 3 days, oxycodone ER 60 mg twice daily and oxycodone IR 15 mg qid since 2009 (MOE = 670 mg). Initially, inpatient detoxification was considered.
- PMH: **Chrohn's disease**, anemia, depression, **poly-substance abuse history**
- Vitals on admission: BP 103/63; HR 96
- Other medications: **oral steroids**, Donnatal®, PPI, lorazepam, mesalamine
 - Discrepant report of patient med use and number of tablets remaining; pt reports meds were stolen by hotel staff

Fentanyl Patch case:

- Taper Plans:
- Due to missing meds, patient had not taken any oxycodone over weekend:
 - Order medications daily
 - Stop oxycodone ER
 - Initially reduce oxycodone IR by one dose (15 mg) to 5 x per day and then reduce in 3 days to 4 doses; then by 7.5 mg qod until 22.5 mg then begin to decrease by 5 mg daily
 - Fentanyl reduce by 50 mcg q3 days until 100mcg; then reduce by 25 mcg q3days x1, then by 12 mcg until off
- Total taper = 27 days

Fentanyl Patch case:

- Patient course:
 - Patient did well with COWS <5 until Fentanyl dose was reduced to 50 mcg/hr and Oxycodone was at 60 mg/day;
 - COWS = 11; BP 113/72; HR 109
 - Began developing increased GI issues of diarrhea; required fluid
 - COWS remained in the 9-18 range with similar BP and HR until end of taper
 - GI symptoms stable; fluids required x1 more episode
 - Patient dismissed to Chemical Dependency program

Oxymorphone Pharmacology:

- Half-life: 7-9.5 hours
- Duration: 4-6 hours
- orphine Oral equivalence = 1:3
- Oxymorphone IR
 - 5 mg and 10 mg tablets
- Oxymorphone ER
 - 5, 7.5, 10, 15, 20, 30, and 40 mg tablets



Oxymorphone Case:

- CM is a 46 yom with chronic chest pain for 20 years following a MVA. He has been on oxymorphone for the past 3 months, but other chronic opioids for the past 10 years. His current dose is 100 mg in three divided doses + oxycodone IR 10 mg four times a day (MOE = 360 mg). PMH: RYGB 2009, Depression, hypoventilation with chronic O2
- Vitals on admission: BP 155/102; HR 75
- Other medications: Duloxetine, pregabalin, vitamins for RYGB

Oxymorphone Case:

- Taper Plans:
 - Reduce oxymorphone by 10 mg per day until 20 mg/day; then reduce by 5 mg daily.
 - Reduce oxycodone by 5 mg daily, until 20 mg/day hold until completion of oxymorphone; then continue to taper by 5 mg/day until done.
- Total taper = 20 days

Oxymorphone / Oxycodone Taper:

| Day | 0600 | 1400 | 2200 | Total dose |
|---------|------|------|------|------------|
| Fri | 40 | 20 | 30 | 90 |
| Sat | 30 | 20 | 30 | 80 |
| Sun | 30 | 20 | 20 | 70 |
| Mon | 20 | 20 | 20 | 60 |
| Tues | 20 | 10 | 20 | 50 |
| Wed | 10 | 10 | 20 | 40 |
| Thur | 10 | 10 | 10 | 30 |
| Fri/S/S | 10 | - | 10 | 20 |
| Mon | 5 | - | 10 | 15 |
| Mon | 5 | - | 5 | 10 |
| Tues | - | - | 5 | 5 |

| Day | 0600 | 1400 | 2200 | Total dose |
|-------|------|------|------|------------|
| F/S/S | 10 | 10 | 10 | 10 |
| Mon | 10 | 5 | 10 | 10 |
| Tues | 10 | 5 | 5 | 10 |
| Wed | 5 | 5 | 5 | 10 |
| Th-W | 5 | 5 | 5 | 5 |
| Thur | 5 | 5 | - | 5 |
| F/S/S | 5 | - | 5 | - |
| Mon | 2.5 | - | 2.5 | - |
| Tues | - | - | 2.5 | - |

Questions?