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BIOMEDICAL AND HEALTH SCIENCES

# Management and Prevention of Opioid Withdrawal


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# Objectives

- Review signs/symptoms of opioid withdrawal
- Review COWS scoring system for opioid withdrawal
- Discuss opioid and non-opioid adjunctive medications for opioid withdrawal
- Discuss prevention of opioid withdrawal, including precipitated withdrawal
- Evaluate example patient cases

# Definitions

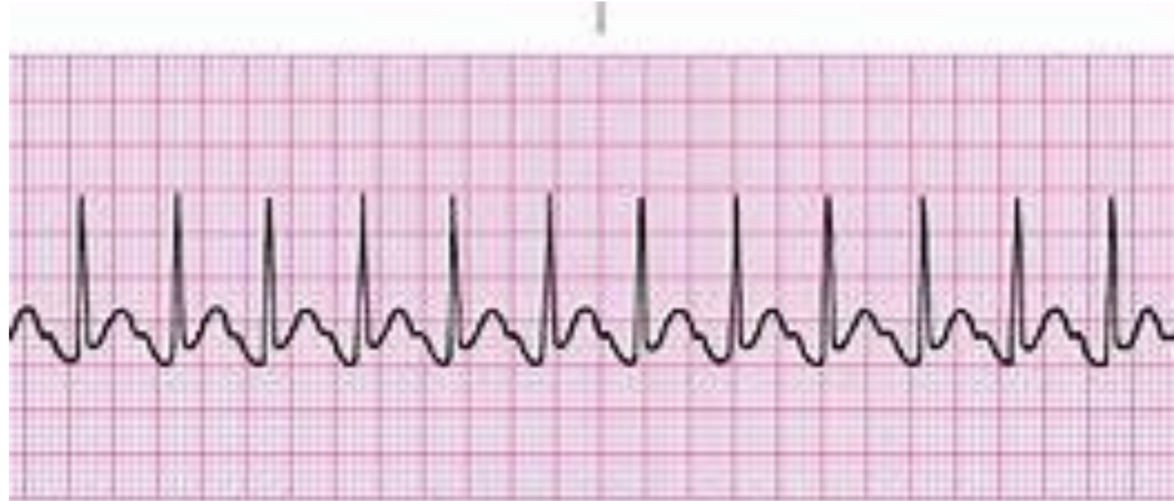
- **Opioid withdrawal**: syndrome associated with the abrupt cessation, or decrease in dosage, of opioids by a patient who has physiologic dependence
- **Precipitated withdrawal:** withdrawal symptoms due to administration of an opioid antagonist or a partial opioid agonist to patient with physiologic dependence on opioids
- **Protracted withdrawal:** signs/symptoms of withdrawal persisting beyond the expected time frame for acute withdrawal, due to changes in neurocircuitry related to chronic opioid use

# Signs and Symptoms of Opioid Withdrawal

- **Objective signs:**
  - Diaphoresis
  - Mydriasis
  - Rhinorrhea
  - Yawning
  - Tremor, agitation
  - Piloerection

# Signs and Symptoms of Opioid Withdrawal, Continued

- Tachycardia
- Hypertension
- Vomiting
- Diarrhea



# Symptoms of Opioid Withdrawal

- Dysphoric mood
- Irritability
- Insomnia
- Pain (generalized, localized, abdominal)
- Some may experience sedation

# Serious Health Implications

- Hypertensive urgency/emergency
- CHF exacerbation due to increased sympathetic tone
- Preterm labor in pregnant women

# COWS Scoring System

- Clinical Opiate Withdrawal Scale
- Classifies opioid withdrawal as mild, moderate, moderately severe or severe
- Based on pulse, diaphoresis, restlessness, pupil size, body pain, rhinorrhea/lacrimation, GI upset, tremor, yawning, anxiety/irritability, rhinorrhea
- Can be used to guide management of opioid withdrawal e.g. when to initiate buprenorphine

# Management of Opioid Withdrawal

- Opioid agonists/partial agonists (preferred!)
  - Methadone
  - Buprenorphine
  - Opioid pain medications

- Non-opioid adjunctive medications (use only in addition to opioid agonists, unless contraindicated/patient preference)
  - Clonidine
  - Antiemetics
  - Antidiarrheals

# Methadone

- Long acting opioid agonist used since 1960s as a treatment for OUD
- Multiple studies have demonstrated safety and efficacy in reducing heroin use, morbidity/mortality, spread of infection, and criminal justice utilization

Joseph, Stancliff, Langrod. Methadone maintenance treatment: a review of historical and clinical issues. Mt Sinai J Med. 2000 Oct-Nov; 67(5-6): 347-64.

# Methadone, Continued

## Advantages

- Easier to initiate than buprenorphine as no risk of precipitated withdrawal
- Does not interfere with opioid pain medications

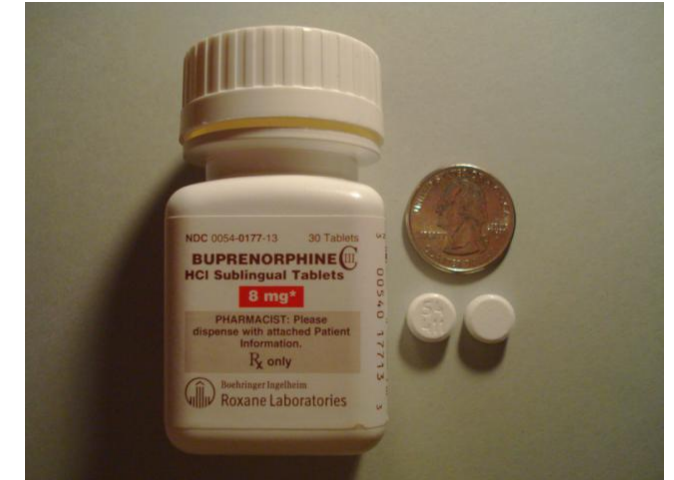
## Disadvantages

- Multiple drug interactions
- QT prolongation (though increased risk of torsades is controversial)
- Does not protect against overdose
- Requires follow up in a methadone clinic

# Methadone, Continued

- Starting dose is 20 – 30mg PO daily
- Dividing doses may provide better analgesic effects
- Titrate up every 3-4 days until improvement in cravings (withdrawal symptoms should resolve with lower dose)

# Buprenorphine




- Partial μ-receptor agonist
- SL tabs/films
- Start with a dose of 2-4mg of buprenorphine when patient exhibits mild-moderate withdrawal
  - Take 2-4mg every 2 hours as needed for a maximum dose of 16mg on day 1
- On day 2, take the total daily dose of day 1 and may divide the dose. Patient can take up to a maximum dose of 24mg on day 2.
- Steady state may take 5-7 days

# Adjunctive Therapies for Opioid Withdrawal

| Withdrawal Symptom | Therapy Options |
| --- | --- |
| Diarrhea | Loperamide |
| Nausea | Ondansetron, Metoclopramide |
| Anxiety, irritability, Diaphoresis | Clonidine |
| Insomnia | Diphenhydramine, Trazodone |
| Pain | APAP/ NSAIDs |

Clinical Resource, *Treatment of Opioid Withdrawal. Pharmacist's Letter/Prescriber's Letter.* August 2018

# Prevention of Opioid Withdrawal

- Continue opioid agonist therapy when possible
  - Hospitalization is a great opportunity to start methadone or buprenorphine in patients with untreated OUD
    - Go low/slow when starting buprenorphine in patients already in mild withdrawal
    - Micro-dosing circumvents need to await withdrawal prior to starting buprenorphine

# Buprenorphine Microdosing

**Table 1. Buprenorphine Microdosing Protocol Used by Our Team**

| Day | Buprenorphine dosage | Methadone dose |
|---|---|---|
| 1 | 0.5 mg[a] SL once/day | Full dose |
| 2 | 0.5 mg[a] SL twice/day | Full dose |
| 3 | 1 mg SL twice/day | Full dose |
| 4 | 2 mg SL twice/day | Full dose |
| 5 | 4 mg SL twice/day | Full dose |
| 6 | 8 mg SL once/day | Full dose |
| 7 | 8 mg SL in A.M. and 4 mg SL in P.M. | Full dose |
| 8 | 12 mg SL/day | Stop |

SL = sublingually.
[a]For our buprenorphine formulation, one-quarter of a 2-mg sublingual strip was used.

**Table 3. Protocol Use in Patient 2**

| Protocol day | Buprenorphine total daily dose, mg | Methadone total daily dose, mg | Maximum pain score, 0–10 |
|---|---|---|---|
| 0 | 0 | 100 | 7 |
| 1 | 1.0 | 100 | 8 |
| 2 | 1.5 | 100 | 6 |
| 3 | 3 | 100 | 8 |
| 4 | 6 | 100 | 7 |
| 5 | 8 | 100 | 8 |
| 6 | 8 | 100 | 8 |
| 7 | 12 | 100 | 6 |
| 8 | 16 | 0 | 6 |
| 9 | 16 | 0 | 8 |
| 10 | 20 | 0 | 8 |
| 11 | 24 | 0 | 6 |

Terasaki, et al. *Pharmacotherapy.* 2019 Oct;39(10):1023-29.

# Prevention of Opioid Withdrawal, Continued

- Discontinuing buprenorphine no longer thought to be necessary perioperatively/for acute pain requiring full opioid agonists
  - Most studies show adequate analgesia from opioid agonists is possible for patients taking 16mg or less buprenorphine/day
  - Continuation of buprenorphine decreases risk of relapse

Goel A et al. The perioperative patient on buprenorphine: a systematic review of perioperative management strategies and patient outcomes. Can J Anaesth. 2019 Feb; 66(2): 201-217.

# Examples

1. 54 year old male with hypertension, opioid use disorder, tobacco use admitted after motor vehicle accident with left femur fracture requiring internal fixation. Post-operative day #1, patient complains of diffuse pain, diarrhea, and irritability. Left leg pain is partially controlled on a Dilaudid PCA.
   - **How do you differentiate between post-operative pain and opioid withdrawal?**
   - **How would you treat opioid withdrawal in this patient?**

# Examples

2. 42 year old female with opioid use disorder and gallstones admitted with acute pancreatitis. Patient is on Suboxone 8-2mg, 1 film SL BID for many years without relapse. Patient complains of severe epigastric/back pain.
    **- Do you continue Suboxone in this patient?**

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