Notes on Pharmacotherapy for Opioid and Alcohol Dependence – March 27, 2023

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Medications for opioid dependence: methadone, buprenorphine, and naltrexone
Medications for alcohol dependence: naltrexone, disulfiram, acamprosate, and gabapentin

Methadone

A synthetic opioid

Commonly misused opioids, such as hydrocodone and heroin:
- Rapid onset → euphoria/high
- Short-acting

Methadone:
- Slow onset → little euphoria/high
- Long-acting - taken once a day for opioid use disorder (OUD)
- Sustains physical dependence
- Addresses other OUD symptoms: preoccupation, urges and cravings, and compulsive use
- The most thoroughly studied and the most effective treatment for any addiction

Federal government regulates closely
- May be prescribed for pain by any clinician with DEA certification
- May be prescribed for OUD only in certified Opioid Treatment Programs

Adverse effects
- Constipation (like all other opioids)
- Interference with sex hormones leading to erectile and menstrual dysfunction

Well-documented long-term benefits
- Prevents HIV/AIDS and hepatitis C and saves lives
- Reduces criminal recidivism

Opioid Treatment Programs/Methadone Programs
- Often include addictions counseling and wrap-around services
- Initial requirement: daily attendance
- Subsequent requirement: 3 times a week

Disadvantages of methadone programs
- Required frequent attendance can hinder work and child care
- Exposure to drug culture in and around the clinic
- Severe withdrawal in newborn when taken by pregnant women

Buprenoprhine (Suboxone®, Subutex®)

A synthetic opioid
- Taken under the tongue twice a day
- Has a ceiling effect, which makes overdose less likely than with other opioids
- Newborn withdrawal is less severe than with methadone

Federal regulations allow prescribing in general healthcare settings
- Previous requirements for training and registration were eliminated in 2023
- Avoids stigma
- Patients can avoid exposure to others with OUD
- Improved access to OUD treatment, especially in rural areas
- Remaining concern: shortage of buprenorphine prescribers nationally

Suboxone contains buprenorphine and naloxone, an opioid blocker
- Naloxone is added to deter misuse by crushing and injecting
- When injected, naloxone enters the bloodstream and blocks buprenorphine
- When taken under the tongue, naloxone is not absorbed into the bloodstream and therefore has no effect
- Recommended for most patients

Subutex contains buprenorphine only
- Recommended for pregnant patients
- Effect of naloxone on developing newborn is unknown

Before starting buprenorphine, patients must stop opioids and be in early withdrawal

First phase of treatment is “induction"
- Patient is observed closely during first week while dose is adjusted
- Some states have a “hub and spokes” model, where hubs do induction

Subsequent phase is “maintenance”
- Visits every 1 week, then 2 weeks, then 4 weeks
- Occasional minor adjustments in dosing

Naltrexone (Revia®, Vivitrol®)

For opioid use disorder, naltrexone blocks opioids
- Opioids taken after naltrexone have little to no effect

The pleasant effects of alcohol rely on several neurochemicals
- Endorphins - natural opioids in the brain that cause runner's high
- Naltrexone blocks the effects of endorphins

- For alcohol use disorder, naltrexone
  > Dulls the euphoria of drinking
  > Blocks urges and cravings to drink

Effective for up to 1 year

Side effects - May cause constipation

Contraindications
- Severe liver disease
- Need to take opioids for pain

Drinking while on naltrexone is not harmful

Pill - once a day - Revia® - also available as a generic

Injection - every 4 weeks - Vivitrol®
- Requires regular visits to a healthcare professional
- Expensive but covered by many health plans
- Net cost savings due to reductions in admissions and ED visits

If patient develops severe pain, opioids must be given in the hospital

Disulfiram (Antabuse®)

Normal breakdown of alcohol in the liver: ethanol → acetaldehyde → acetic acid
Disulfiram blocks the breakdown of acetaldehyde to acetic acid
High levels of acetaldehyde can cause nausea, vomiting, flushing, and death

Taking disulfiram once a day deters drinking for 24 to 48 hours

Contraindications: severe liver disease, certain but not all heart diseases

Must be given with patient's consent

US experience - Poor long-term effectiveness; craving leads to non-adherence - May be effective in the short term for impulsive or highly motivated individuals

Studies in Europe suggest effectiveness similar to other medications

Especially effective if administration is supervised

Acamprosate (Campral®)

<u>Acute alcohol withdrawal</u>
- Agitation, tremors, nausea, vomiting, hallucinations, seizures, disorientation
- Lasts up to 7 days

Then <u>subacute withdrawal</u> occurs for several weeks to 12 months
- Difficulty sleeping, anxiety, restlessness
- Symptoms often trigger desire to drink

Acamprosate reduces the symptoms of subacute withdrawal

Must be taken 3 times a day

Side effects
- Sometimes causes diarrhea in the first week
- Avoid diarrhea by halving the dose for the first week
- May aggravate depression and lead to suicidality

May be taken with severe liver disease

Gabapentin (Neurontin®)

FDA-approved for partial seizures, neuropathy, and restless legs

Not FDA-approved for alcohol dependence, but several studies suggest effectiveness
- Fewer cravings
- Longer abstinence
- Less relapse to heavy drinking

Might be more effective for patients who have had severe alcohol withdrawal

Usually dosed 3 times a day

Many but usually mild side effects
- Drowsiness, dizziness, and weakness are common
- Such side effects are worse with alcohol

May increase suicidal thoughts

Rare liver toxicity - may be taken by patients with liver disease if liver function is monitored by blood tests