Polysubstance use in OAT patients

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Faculty/Presenter Disclosure

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  - *None*

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Mitigating Potential Bias

- No commercial interests but I will use generic names and try to mention when a product is being used “off-label”

Learning objective

Review polysubstance use, especially in the context of OAT:

- Alcohol
- Cannabis
- Benzodiazepines
- Stimulants (Cocaine, Crystal methamphetamine)
- Opioids

Case study

- 34 year-old man works in snow removal/landscaping, stable on buprenorphine 24mg x 2 years for previous addiction to heroin, oxycodone, ivdu
- After work, goes home and has 4-7 drinks, smokes one joint, and a few times a week will use one of his partner's 2mg ativan Rx
- If he's had a physically taxing day he will use some hydromorphone or fentanyl
- Uses cocaine with fentanyl in a social setting on most Saturday nights
- Has missed several days of work – attributes to being hungover - and is worried about losing his job

Alcohol use disorder

- Alcohol use disorders are prevalent in the general population
- NIAA: 7.5% in men, 4% in women
- One of the most common substances: legal, socially acceptable

- **What is the prevalence in patients on OAT?**

OAT and the prevalence of AUD

Varying studies but significantly higher than general population:

- **Irish**: 35% in MMT patients
- **British**: >1/3 in community OAT, >1/2 in residential OAT programs
- **Swiss**: 38-47% alcohol abuse, 20-24% daily alcohol use
- **Australian**: 41% AUDIT positive but only half believed they had a problem with alcohol
- **Germany**: 28% daily alcohol use

Concurrent opioid and alcohol use disorder

- Often goes undetected as we don't routinely check UDS and many of our patients don't go for bloodwork (low plts, elev LFTs, MCV, **Hep C**)
- Probably first line is buprenorphine for OAT if alcohol an issue
- Some patients drink alcohol in part for relief of opioid withdrawal symptoms
- Relieving opioid withdrawal can reduce alcohol consumption

Naltrexone

- First line treatment for patients **not** on OAT
- **Cannot be used in OAT patients as it is an opioid antagonist**
- Blunts reinforcing effects of alcohol, reducing cravings
- Dosing range 25-100mg, start at 25mg, increase to 50mg, up to 100mg
- Monitor LFTs and discontinue if they rise > 3 x above baseline
- But risk of ongoing drinking outweighs theoretical risk of liver damage
- Naltrexone (LU 532)

Acamprosate

- Acamprosate –first line treatment esp in OAT
- Relieves subacute withdrawal symptoms
- Several double blind placebo RCTs demonstrating effectiveness
- However, hasn't been available since April 2019
- Best for patients with more severe AUD/withdrawal
- 666mg tid

Disulfiram

- Affects ethanol metabolism by irreversibly inhibiting acetaldehyde dehydrogenase resulting in build up of acetaldehyde metabolites
- This causes palpitations, diaphoresis, flushing, nausea, tachycardia
- Very good at craving extinction (titrating to fear)
- Early studies show promise for cocaine: inhibits DBH, an enzyme that converts DA to NA, results in accumulation of DA

Disulfiram

- Contraindicated in CAD, heart failure
- Rare but serious hepatotoxicity – baseline and regular LFTs – weigh risks vs benefits in patients with liver disease
- Not ODB covered, need compounding pharmacy, about $80 per month
- Dosing ranges from 125-500 mg per day and need to be abstinent x12 hours minimum, abstain 2 weeks after

Gabapentin

- Can be used to tx mild withdrawal acutely or for maintenance to tx ongoing subacute mild withdrawal
- Doses 900-1800mg although higher doses hard to tolerate
- Excreted via kidney so monitor renal function
- Increased risk of OD with opioids so caution with OAT patients and use only if concurrent disorder e.g. anxiety, neuropathy
- Also can be a drug of abuse

Odansetron

- Might be useful for early onset alcoholics (< 25 years)
  - 5HT3 receptor blocker usually used for nausea
  - 3 RCTS – shows some benefit in younger patients (?genetic basis)
  - Usually have severe, destructive history of AUD
  - 4mg bid but optimal dose not known – trials used different doses

Baclofen

- Results are mixed
- Three trials: two (n=39, 84) found a difference, one found no difference (n=80)
- Dose range is 20-60mg per day divided in three doses
(Higher doses not more effective and more poorly tolerated)
- Inexpensive and could consider as an option for someone without coverage

Varenicline

- Approved for nicotine dependence but studies have shown it modulates dopamine release in the nucleus acumbens
- Controlled trials suggest varenicline reduces drinking when given to smokers who also drink heavily
- Titrate up to 1mg bid
- Potential option for patients are are also nicotine dependent

SSRIs

- Two metanalyses on AUD in patients with comorbid depression and SSRI had opposite results – one found SSRIs reduced drinking, another did not.
- Reasonable to use if comorbid depression or anxiety

Combination therapy

- If inadequate response to monotherapy
- All trials involve naltrexone which is not an option for OAT patients

Mixed results
- Three combinations studied:

Naltrexone/acamprosate: mixed results – COMBINE no advantage

Naltrexone/odansetron: combination was effective, but not compared to monotherapy!

Naltrexone/SSRI: only more effective if depressed

Thiamine

- High dose may be more effective than lower dose, though very little evidence

- IV/IM – better absorption

- Recommendation:
  - Vary by country
  - Range from 200-500 mg IM/IV x 3-5 days, followed by 100 mg OD x 1 month

Managed alcohol programs

- Some results showing benefit (cohort studies)
- ThunderBay, Hamilton, Sudbury, Toronto
- For severe AUD (10+ standard drinks per day)
- Regularly drinks non-palatable alcohol (e.g., mouthwash, hand sanitizer)
- No response to an adequate trial of anti-alcohol medication
- Frequent emergency department visits
- Unable to participate or didn't respond to psychosocial AUD treatment
- Unstably housed or homeless

Cannabis

- Screen your patients for:
  - recreational use vs
  - problematic use vs
  - a cannabis use disorder
- Harm reduction advice (e.g. driving, frequency of use, route)
- If have a cannabis use disorder, offer tx
  - CBT
  - MI
  - contingency management depending on clinical situation
- No evidence-based pharmacotherapy although some studies showing treating sleep/anxiety with gabapentin, buspirone, zopiclone

Opioids

- First line tx for OUD is OAT (MMT, bup, SROM)
- But what if patients continue to use opioids despite being on OAT?
  - Dosing?
  - Resistance to optimal dosing often changes with counselling, therapeutic bond
  - Consider transition to another OAT (e.g. bup to MMT)
  - Alternative/adjuvant opioids?

Methadone dosing

- Guidelines were written "pre-fentanyl"
- Dose? Consider higher methadone doses than guidelines
- QT prolongation? Can monitor with EKG: series of case reports showed 517-626 was range at which torsades occurred, 25% were also on lower doses methadone - ?Levomethadone
- RFs: female, SSRIs, age
- Trial of one or two dose increases to see if it helps
- Risk of fentanyl vs increased methadone dosing

Slow release oral morphine (SROM)

- For patients who have failed at or can't tolerate methadone and buprenorphine or possibly as an adjuvant to other OAT
- Less evidence on SROM, and is harder to monitor with UDS
- Can be injected; should have daily observed dosing
- Morphine microgranules should be sprinkled on yogurt or in juice
- Initial dose 60-120 mg; maintenance dose 200-800 mg/day
- Titrate to relieve withdrawal symptoms, cravings and opioid use

HMT

- Controversy "Safe supply"
- Take home HMT : avg dose is 8mg x 14 tabs/d– up to 21 tabs/d
- Not observed – might be daily dispensed
- Case reports of increase IE, cellulitis, candidemia, street supply
- Research underway but no research as of yet as evidence is for iOT which is very different (structured, observed)

OAT in France: MMT vs Bup vs Morphine

- Study of 1,000 patients on take-home morphine, 20,000 patients on buprenorphine and 9,000 patients on methadone, between 2012 and 2014, using the French Nationwide Healthcare Data System (Bertin 2019)
- Morphine group had:
  - 9 x mortality rate vs buprenorphine, 2x mortality rate vs methadone
  - 4 x higher rate of hospitalizations for overdoses
  - 2.8-3.6 higher rates of hospitalization for bacterial infections
- Authors attribute the results to unsupervised injection of morphine
- French subjects were using heroin not fentanyl

iOT

- There is evidence supporting Injection Opioid Therapy (IOT)
- IOT differs from HMT in a few fundamental ways:
  - IOT only accepts patients with documented evidence of continued use of illicit opioids despite an adequate trial of OAT
  - Methadone is offered onsite
  - All injections are supervised by a trained health care professional at the clinic site to prevent diversion, ensure sterile technique and safety

Pharmacotherapy for:

STIMULANTS:
COCAINE AND CRYSTAL METHAMPHETAMINE

Pharmacotherapy for Stimulant Use Disorders

- No approved pharmacotherapy, most of it is experimental with mixed results and some promising results but in smaller trials
- Standard of treatment: Counselling

Anticonvulsants

- Cochrane review:
  - 20 studies
  - N=2068, mean age 36
  - Outpatients, 8-24 weeks
  - Topiramate, gabapentin, lamotrigine, phenytoin, vigabatran
  - Anticonvulsant vs placebo

Conclusion: Not effective, increased SEs

Topiramate trials: non effectiveness correlated with OUD patients, one trial on MMT patients found topiramate no better than placebo

DA agonists

- Similar to the idea of OAT or NRT
- Cocaine seems to involve multiple transmitters: mixed results
- Several trials in Cochrane review: amantadine, bromocriptine, Levodopa, pramipexole, pergolide, cabergoline hydergine
- The trails were short with mean duration of 7 weeks
- DA agonist vs placebo: no evidence for use of DA agonists

Antipsychotics

- Controlled trials show that antipsychotics are effective at reducing acute psychotic symptoms and retaining patients in treatment, but not at reducing crystal meth or cocaine use
- Olanzapine and risperidone most effective antipsychotics for acute psychosis in stimulant use

Stimulants

- Cochrane Review: 26 studies, n=2366, mean age 39.6, 6-24 weeks
- Nine meds: dexamphetamine, lisdexamfetamine, methylphenidate, modafinil, methamphetamine, amphetamine salts, selegiline, mazindol
- Trials did not demonstrate sustained abstinence from cocaine or crystal meth, or improvements in mood, crime rates, employment
- Conclusion: low quality evidence - stimulant therapy not recommended given risks (diversion, injection, cardiovascular complications, psychosis) but further research warranted because of some promising results in small trials

Stimulants

- A trial of stimulants may be considered in patients who are engaged in psychosocial treatment and are highly motivated to quit but have strong cravings and periodic use
- Cocaine: most evidence for modafinil (used for narcolepsy) and lisdexamfetamine (Vyvanse), amphetamine salts (Adderall)
- Crystal meth: modafinil and buproprion
- These agents are not more effective than other stimulants, but have less potential for abuse

Stimulants and ADHD

- ADHD appears to be a risk factor for stimulant use disorder
- ADHD is a difficult diagnosis to make in adult stimulant users
- Use a formal validated tool

Stimulants and ADHD

- Two small RCTs have shown that stimulants reduce stimulant use and improve ADHD symptoms in patients with ADHD
- Intervention meds: Mixed amphetamine salts 60, 80 mg; methylphenidate up to 180 mg
- Check patient's cardiovascular and psychiatric status
- Therapeutic trial: Discontinue if no clear and convincing evidence of decreased stimulant use, through UDS and self-report

Harm reduction and stimulant use

- Harm reduction kits: Pyrex system for crack smoking, lip balm
- Do regular UDS for fentanyl: warn re risks, naloxone kit
- Consider naltrexone if not on OAT – may reduce cocaine use and has high affinity for receptor so may protect against fentanyl overdose
- Strong association between stimulant use and high risk sex
- Counsel patients on safe sex (PnP associated with HIV transmission)

Counselling

- Strongest evidence is actually for CM (studies were voucher based for goods though, not in the OAT context of carries etc but may be similar)
- CBT more effective than standard supportive counselling but Cochrane review: All forms of counselling have been shown to be more effective than no counselling
- Some evidence for IPT, MI

BENZODIAZEPINES

Therapeutic use of benzodiazepines

- Many with a substance use disorder are on therapeutic doses of benzodiazepines although not indicated for LT use
- Tapering usually indicated, although it may not be the top priority clinically
- Tapering may:
  - Improve mood, energy, sleep
  - Reduce risk of adverse drug interactions eg falls, sleep apnea from opioid/benzo or alcohol/benzo combinations

Approach to benzodiazepine taper

- Could use same benzo or convert to ½ - 2/3 the equivalent dose of clonazepam; adjust up or down according to symptoms
- Diazepam 5mg = lorazepam 0.5-1mg = clonazepam 0.5-1mg
- Scheduled dosing
- Flexible, slow reduction based on patient negotiation
- Patients will feel better with tapering – more alert, energetic, better mood

Tapering therapeutic doses

- Goal is not always zero especially if it has been many years and there's a significant underlying anxiety disorder
- If subacute withdrawal may respond to SSRIs, SNRIs, pregabalin
- See patient regularly, provide supportive counselling
- Group and individual psychotherapy can also be helpful, eg CBT

Benzodiazepine use disorder

- Taper with clonazepam, daily dispensed if the patient acquires benzos from multiple sources
- Monitor via UDS (chromatography) – stop if outside sources
- Could use gabapentin, pregabalin, paroxetine, TCA

COUNSELLING

Counselling

- **Influence of trauma:** People with a **history of trauma or adverse childhood events** have high levels of anxiety, depression, and suicidality. Using substances can help people to cope with these feelings and allow them to feel at ease

- **Paradox of drug use**: Sometimes the patient can't imagine life without the substance because they cause powerful but temporary relief of anxiety, and withdrawal markedly increases anxiety. But anxiety improves dramatically with abstinence.

Trauma informed care

- Providers should recognize and explain the role of trauma in substance use disorders
- Emphasize the patient's resilience and successes despite the impact of trauma
- Encourage connect to trauma programs

Domestic violence

- Ask patients about violence
- If physical violence present, discuss options:
- Programs for victims of domestic violence
- Shelter or WMS or stay with a friend
- Encourage patient to contact police, and collect evidence
- Discuss concerns about police contact
- Emphasize that abstinence will make it easier

Strong therapeutic bond

- This is critical for effective counselling; has a major impact on treatment retention and outcome
- At least one member of a team with an ongoing relationship with the patient – could be physician, nurse or case manager
- Not based on any one technique - bond is formed when therapist shows empathy, honesty, regard for the patient
- Patient needs to feel that they are not judged

Back to the case

- Did a trial of disulfiram as immediate abstinence desired because on probation at his job – considered varenicline
- Started him on buproprion to potentially help with stimulant use, depression
- Increased counseling for his cannabis use and stimulant use
- Increased dose of buprenorphine to 26mg

Back to the case

- Disufiram was very effective for him but increase LFTs/bili
- Still uses benzos periodically for anxiety, relaxation
- Cannabis use continues but less frequently
- Cocaine use continues – buproprion not effective, but mood is better
- Overall, less opioid use with increase buprenorphine dose
- Overall feels he is doing better, has been able to keep his job so far, few relapses to binge drinking but less frequent

Thank you!

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