MEDICATION-ASSISTED TREATMENT FOR SUBSTANCE USE DISORDERS

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Objectives

- Identify best medication regimens for safe withdrawal from opioids
  - Buprenorphine
  - Methadone
  - Buprenorphine/naltrexone
  - Supportive medications
- Identify best medication regimens for treatment of opioid addictions
  - Buprenorphine
  - Buprenorphine/naltrexone
  - Methadone
  - Supportive medications
- Identify supportive medications and therapies for continued recovery
  - Nightmare medications
  - Sleep aids
  - Therapies and supportive resources

TERMS

- Addiction – treatable, chronic medical disease involving complex interactions among brain circuits, genetics, the environment and individual's life experiences
- Diversion – unauthorized or misappropriation of prescription medication to someone other than for whom it was intended
- Misuse – taking a medication in a manner other than was prescribed
- Opiate – one of a group of alkaloids derived from the opium poppy with ability to induce analgesia, euphoria and in higher doses, stupor, coma and respiratory depression; exclude synthetic opioids
- Opioid - psychoactive chemical that resembles morphine in pharmacological effects, including opiates and synthetic/semisynthetic agents that exert their effects by binding to highly selective receptors in the brain where morphine and endogenous opioids affect their actions
- Opioid agonist medication – pharmacologically occupy and activate opioid receptors in the body; relieve withdrawal symptoms and reduce or extinguish cravings for opioids
- Opioid antagonist medication – pharmacologically occupy opioid receptors but do not activate the receptors; effectively blocks receptor, preventing brain from responding to other opioids; further use of opioids does not produce analgesia, euphoria or intoxication
- Opioid use disorder – a substance use disorder involving opioids

TERMS CONTINUED

- Opioid withdrawal syndrome – rebound hyperexcitability; craving, anxiety, dysphoria, yawning, sweating, piloerection, lacrimation, rhinorrhea, insomnia, nausea or vomiting, diarrhea, cramps, muscle aches and fever
  - Short acting drugs – morphine or heroin; withdrawal symptoms appear within 8-12h of last dose, peak at 48-72h and clear after 7-10 days
  - Longer acting drugs – methadone; withdrawal may not occur until 1-3 days after last dose, peak between third and eighth day and may persist several weeks
- Overdose – inadvertent or deliberate consumption of a dose much larger than that either habitually used by the individual or ordinarily used for treatment of an illness that results in serious toxic reaction or death
- Recovery – process of sustained action that addresses the biological, psychological, social and spiritual disturbances inherent in addiction
- Relapse - process in which an individual who has established disease remission experiences recurrence of signs and symptoms of active addiction, often including resumption of the pathological pursuit of reward and/or relief through the use of substances and other behaviors

WHAT WE KNOW...

- Opioids include morphine, heroin, oxycontin, codeine, methadone and hydromorphone hydrochloride
- 3 types of opioid receptors: mu, delta, kappa; mu receptor is crucial for reinforcing actions of opioids
- Comprehensive assessment is imperative including mental health status and co-occurring with other substances
- Use of cannabis, stimulants, alcohol and/or other addictive drugs should not be reason to withhold or suspend opioid use disorder treatment
- Use of benzodiazepines and other sedative-hypnotics should not be reason to withhold or suspend treatment with methadone or buprenorphine
- A nicotine use query should be completed routinely and counseling on cessation provided
- Assessment of social and environmental factors to identify facilitators and barriers to treatment and long-term recovery
- Addiction is a complex biopsychosocial illness

SYMPTOMS OF WITHDRAWAL

- Generally self-diagnosable and not life threatening
- May use COWS – Clinical Opiate Withdrawal Scale
- Common symptoms:
  - GI – diarrhea, vomiting, nausea, abdominal pain
  - Whole body – restlessness, sweating, muscle pain, piloerection, tremor
  - Mood – general discontent, anxiety, irritability
  - Eyes – dilated pupils, watery
  - Other – fast heart rate, excessive yawning, insomnia

QUESTION #1

Opioid withdrawal symptoms may include:

A. Hunger, constipation, irritability

B. Yawning, cramps, sweating

C. Sleeping more, hypothermia, hot flashes

SIGNS OF POTENTIAL DIVERSION

- Request early refills
- Inconsistent lab results
- Claim allergic to naloxone, request mono therapy
- Police reports indicating selling on streets
- Reports of concerning behaviors from family, friends, pharmacy, etc
- Inconsistent appointments

ASSESSMENT AND DIAGNOSIS OF OPIOID USE DISORDER

- Comprehensive assessment is critical for treatment planning
  - Medical history screening for concomitant medical conditions including psychiatric disorders, infectious diseases, acute trauma and pregnancy
  - Physical examination
  - Initial laboratory testing – CBC, liver enzymes, TB, Hep B & C & HIV, STDs, pregnancy
- Completion of all assessments SHOULD NOT delay or preclude initiating pharmacotherapy

TREATMENT OPTIONS

- All FDA approved medications for the treatment of opioid use disorder should be available to all patients
- Clinicians should consider the patient's preferences, past treatment history, current state of illness and treatment setting when deciding between use of methadone, buprenorphine and naltrexone
- No recommended time limit of pharmacological treatment
- Patient's decision to decline psychosocial treatment or absence of available psychosocial treatment should not preclude or delay pharmacotherapy with appropriate medication management
- Clinicians should consider psychosocial situations, co-occurring disorders and risk of diversion

QUESTION #2

Your female patient with an established diagnosis of opioid use disorder declines psychosocial treatment. You should

A. Decline all treatment telling her to return when she agrees

B. Delay pharmacotherapy treatment until she enrolls in an outpatient treatment program

C. Initiate pharmacotherapy treatment as soon as possible

METHADONE

- Full mu-opioid agonist
- Higher levels of physiological dependence
- Can only be provided in opioid treatment programs and acute care settings
- For withdrawal from short acting opioids, initial dose should be 20-30mg per day and tapered off in 6-10 days
- Initial dose 10-30mg, reassess in 2-4h; use lower dose 2.5 to 10mg individuals with no or low opioid tolerance
- Usual daily dose ranges 60-120mg, do not increase daily, typically increase by no more than 10mg every 5 days; long half-life
- Maintenance better at 6-120mg/day
- Administration should be monitored due to misuse and diversion
- Previous treatment should be reinstituted immediately if relapse occurs
- Transitioning to buprenorphine should be low dose methadone (30-40mg)
- Transition to naltrexone requires complete withdrawal
- No recommended time limit for pharmacological treatment
- Discontinuance of treatment increases risk of opioid overdose and overdose death if return to illicit use

METHADONE WARNINGS AND PRECAUTIONS

- Head injury and increase intracranial pressure
- Liver disease
- Respiratory insufficiency
- Cardiac conduction effects
- Drug interactions
- Interactions with antidepressants and migraine meds leading to serotonin syndrome
- Contraindicated with hypersensitivity, respiratory depression, severe bronchial asthma or hypercapnia or paralytic ileus
- Arrhythmias; QT prolongattion

BUPRENORPHINE

- Partial mu-agonist
- Can be prescribed by waivered clinicians in any setting
- Relieves drug cravings without euphoria
- Withdrawal management not initiated until there are objective signs of opioid withdrawal
- Dose sufficient to suppress withdrawal symptoms (initial dose of 2-4mg titrated up as needed to suppress withdrawal symptoms
- Increase in increments of 2-8mg; titrate to alleviate symptoms and discontinue illicit opioid use
- 16mg/day or more may be more effective than lower doses; limited evidence regarding efficacy of doses higher than 24mg/day
- Higher doses may increase risk of diversion
- Setting carefully considered – office-based and home-based
- When transition to naltrexone, 7-14 days should elapse
- When transition to methadone, no required time delay
- No recommended time limit for pharmacological treatment
- Taper and discontinuation is slow process, close monitoring, over several months
- Generally recommend combination buprenorphine/naloxone

BUPRENORPHINE WARNINGS AND PRECAUTIONS

- Hypersensitivity
- Severe hepatic impairment
- May cause sedation
- Physical dependence
- Risk of life-threatening respiratory depression and death when used with benzos or other CNS depressants like alcohol, other opioids, and illicit drugs
- Precipitated withdrawal if used with physically dependent on full agonists opioids before agonoist effects have worn off
- Interaction with antidepressants and migraine meds can cause serotonin syndrome
- Addison's disease, rare
- Diversion and misuse
- Neonatal withdrawal after use during prregnancy

BUPRENORPHINE FORMULATIONS

- Suboxone or generic sublingual tablet
- Suboxone or generic sublingual film
- Zubsolv sublingual tablet
- Bunavail buccal film
- Cassipa sublingual film
- Generic equivalent of subutex sublingual tablet
- Sublocade subcutaneous injection
- Brixadi IM or deep SC injection

NALTREXONE

- Antagonist
- Can be prescribed in any setting by any clinician with authority to prescribe medicine
- Oral naltrexone is often adversely affected by poor medication adherence so should not be used except under very limited circumstances
- Extended-release injectable naltrexone reduces issues with medication adherence
- Extended-release injectable every 4 weeks, deep IM, 380mg; every 3 weeks for rapid metabolizers
- No recommended length of treatment
- Transitioning to methadone or buprenorphine is less complicated as no physical dependence and no possibility of precipitated withdrawal
- Increased risk of opioid overdose with discontinuance

NALTREXONE WARNINGS AND PRECAUTIONS

- Hypersensitivity
- Active hepatitis
- Current physical dependence on opioids; receiving opioids; acute opioid withdrawal
- Vulnerability to overdose
- Injection site reactions
- Precipitated opioid withdrawal
- Caution with thrombocytopenia or coagulation disorder
- Risk of hepatotoxicity
- Monitor for depression and suicidality
- Eosinophil pneumonia with injectable
- Emergency reversal of opiate blockade may require critical care setting
- No evidence of safety during pregnancy

QUESTION #3

Your client John wants to try naltrexone for his opioid use disorder. Naltrexone is contraindicated if John

A. Is in acute opioid withdrawal

B. Passed the naloxone challenge

C. Previously took naltrexone but relapsed after stopping

NALOXONE

- Short-acting opioid antagonist
- Antagonist
- For the reversal of opioid overdose
- Provide to patients being treated for or with a history of opioid use disorder
- Train patients and family members/significant others in use

OPIOID WITHDRAWAL DO'S AND DON'TS

- Use methadone or buprenorphine over abrupt cessation of opioids
- Abrupt cessation may lead to strong cravings, and/or acute withdrawal syndrome putting patient at risk for relapse, overdose and overdose death
- Opioid withdrawal management/detoxification is not recommended with ongoing treatment
- Ongoing maintenance medication in combination with psychosocial treatment appropriate for patient's needs is standard of care

OTHER ASSISTIVE MEDICATIONS

- Alpha-2 adrenergic agonists (lofexidine and off-label clonidine) safe and effective but less effective in reducing symptoms of withdrawal, retaining patients in withdrawal management and supporting completion of withdrawal
- Loperamide for diarrhea
- Promethazine for nausea/vomiting
- Ibuprofen or naproxen for myalgia
- Clonidine for elevated b/p

ACTIVE CO-OCCURRING ALCOHOL OR SEDATIVE, HYPNOTIC OR ANXIOLYTIC USE DISORDER

- May need a more intensive level of care than can be provided in office-based setting
- Carefully monitor individuals who are regularly using alcohol or other sedatives
- Use benzodiazepines and other sedative-hypnotics cautiously as increases risk of serious side effects

INDIVIDUALS WITH PAIN

- Non-opioid medications with pain modulating properties
- Behavioral approaches
- Physical therapy
- Procedural approaches
- Non-opioid analgesics
- Methadone or buprenorphine should be considered, stabilized and managed concurrently
- Temporarily increasing dose or dosing frequency may be effective (split dosing)
- With methadone, add short acting full agonist opioid to manage moderate to severe acute pain; anticipated to be higher dose
- With buprenorphine, may benefit from addition of as-needed doses; addition of short-acting full agonist opioid
- Discontinuation of methadone or buprenorphine before surgery not required;
- Higher potency IV full agonists opioids can be used perioperatively

SIGNS OF POTENTIAL DIVERSION

- Request early refills
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DIVERSION PREVENTION

- Frequent office visits especially at beginning of treatment and until stable
- Drug testing, buprenorphine and metabolites and use of illicit and controlled substances
- Recall visits for medication counts

RELAPSE PREVENTION

- Important part of addiction treatment

CLINICIAN QUALIFICATIONS – APRN/PA

- Licensed to prescribe schedule III, IV or V meds for treatment of pain
- Obtain no fewer than 24 hours of initial training
- Have such other training or experience that demonstrates the ability to treat and manage patients with opioid use disorder
- Be supervised by or work in collaboration with qualifying physician if required by state law

REFERENCES

- https://www.drugabuse.gov/drug-topics/opioids/opioid-summaries-by-state/oklahoma-opioid-involved-deaths-related-harms
- The ASAM National Practice Guideline for the Treatment of Opioid Use Disorder, 2020 Focused Update
- https://www.mcbi/nim.nih.gov/books/NBK526012

Questions?