Medication-Assisted Treatment for Adolescents

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Objectives
- Describe how medication-assisted treatment fits into the context of overall addiction treatment, including for adolescents
- Recognize some advantages and limitations of medication-assisted treatment among special populations (dual diagnosis, pregnancy) of adolescents
- Discuss pharmacotherapy for treatment of opioid use disorder, tobacco use disorder, and alcohol use disorder

Overview
- Overview of Medication-Assisted Therapy
- Lunch
- Pharmacotherapy for Opioid Use Disorder
- Small group case discussions
- Pharmacotherapy for Tobacco Use Disorder
- Break
- Small group case discussions
- Pharmacotherapy for Alcohol Use Disorder
- Small group case discussions
- Wrap-Up
Medication-Assisted Therapy

Long-Term Pharmacotherapy for Substance Use Disorders

- Doesn’t cure substance dependence
  - Helps reduce drinking or episodes of use
  - Achieve longer abstinence
- Works for a proportion of patients
- Goals
  - Increase time to relapse
  - Reduce intensity of binge if relapse occurs

Clinical Use of Pharmacotherapy

- Part of comprehensive plan that addresses psychological, social, & spiritual needs
- Do not use in place of counseling
- Works best in combination with psychosocial support
Behavioral Treatment

- Essential component of addiction treatment
- Multiple modalities available
- Multiple settings
  - Outpatient is most common
- Can be used alone or with pharmacotherapy

12-Step Groups

- Narcotics Anonymous
  - Based on Alcoholics Anonymous
- Group format
- Anonymous
- No cost
- No affiliations or endorsement
- Different groups have different characteristics

Other Addiction Counseling

- Motivational Enhancement
- Cognitive-behavioral Therapy
- Relapse Prevention
- Network therapy
- Family therapy
- Supportive psychotherapy
- Twelve-Step facilitation
- Rational Recovery
- Matrix Model
- Medication Management
- Brief Intervention
Factors to consider

- Whether to add long-term pharmacotherapy
- No pharmacotherapy for most classes of abused drugs
  - Stimulants
  - Hallucinogens
  - Inhalants
  - Marijuana

Cost  
Availability  
Side effects  
Other meds taken  
Motivation

Adherence

- Medication must be taken consistently to be effective
- Challenging with long-term pharmacotherapy for addiction
  - Many are not immediately rewarding
- Requires sustained motivation
  - Counselors and advocates help with this

What is the endpoint?

- Duration of most long-term pharmacotherapy is not indefinite
  - Months to years
- Goal is stabilization
  - Flexibility
  - Individualized
  - Allow for relapse
Addiction in Adolescents
- Pattern of use
  - Shorter duration
  - Fewer consequences
- Protection from consequences
  - Family
  - Legal (Juvenile Justice System vs. adult courts)
- Immaturity
  - Don’t recognize problem
  - Habilitation, not rehabilitation

Substance Use Disorders in Adolescents
- More difficult to treat
- Higher relapse rates
- Worse outcomes
- Increased risk for injuries and violence

SUD Pharmacotherapy in Adolescents
- Medications that are regular component of adult treatment are not often used in youth
- Lack of FDA approval
- Not a lot of published data
- Youthful experimentation may not lead to full SUD
Opioid Painkillers

**Short-acting**
- Tylenol #3 (codeine)
- Darvon (propoxyphene)
- Vicodin (hydrocodone)
- MSIR (morphine)
- Percocet (oxycodone)
- Dilaudid (hydromorphone)
- Fentora (fentanyl)

**Long-acting**
- MS Contin (morphine)
- OxyContin (oxycodone)
- Opana ER (oxymorphone)
- Dolophine (methadone)
- Duragesic (fentanyl)
- Exalgo (hydromorphone)

Opioid effects

- **Analgesia**
  - Dissociation from pain
- **Euphoria**
  - Dissociation from anything/everything unpleasant
- **Sedation**
  - Reduction of anxiety
- **Smooth muscle relaxation**
  - Nausea
  - Constipation
- **Vasodilation**
  - Low blood pressure
  - Headache
- **Histamine release**
  - Itching
- **Cough suppression**

Opioid Use in Adolescents

- **2015 data**
  - 276,000 adolescents were current nonmedical users of opioid painkillers
  - 122,000 having an addiction to prescription pain relievers
  - 21,000 adolescents had used heroin in the past year
  - 5,000 were current heroin users
- **Admissions for opioid addiction treatment have increased**
Opioid Use Progression

- Most adolescents who misuse prescription pain relievers are given them for free by a friend or relative
- 4/5 new heroin users started out misusing prescription painkillers
- 94% of people in treatment for opioid addiction said they chose to use heroin because prescription opioids were “far more expensive and harder to obtain.”

Tobacco

- Cigarettes, cigars, pipes
  - Many different harmful compounds
- Smokeless tobacco
  - “snuff,” “chew”
- Stimulant & relaxes
- Acute effects
  - Vasoconstriction
- Very short-acting, so high-frequency use
  - Very reinforcing

Electronic cigarettes

- Neither designed nor marketed for smoking cessation
- Intentionally attractive to youth with flavorings (bubblegum, etc.)
- Only recently became regulated in U.S.
- Less harmful than tobacco, but more dangerous than air
Smoking rates

- Tobacco & weight
  - Girls concerned about their weight start smoking at higher rates than boys
- 13% of adolescents smoke ½ pack/day
- Up to 24% of girls and 30% of boys have ever used e-cigarette
  - 7- to 10-fold increase from 2011 to 2015

Why is it so hard to quit smoking?

- Nicotine is as addicting as heroin, cocaine, or alcohol
- Stimulation of nicotine receptors in the brain & activation of the dopamine reward system mediate the pleasurable effects and positive reinforcement

Why is it so hard to quit smoking?

- The behaviors of seeking, lighting, & self-administering cigarettes become entrenched in daily routine
- Nicotine has become important in modulation of mood, appetite, energy metabolism, and ability to deal with stress & boredom
Alcohol

- CNS depressant
- Disinhibition
  - Depress inhibitions first
  - Reduce anxiety
  - Fun at parties
- Socially acceptable
- Readily available
  - Not illegal
  - Obtain from older peers

Epidemiology

- Most teens use alcohol occasionally without consequences
  - 80% of high school students have used alcohol
- Problem behavior
  - 35% of 12th graders binge drink at least once a month
  - 4% of adolescents drink daily

Alcohol use & abuse

- Prevalence of alcohol disorders highest among young adults
- Risk factors for alcohol dependence
  - Male
  - Younger age
  - Family history
  - Unemployment
  - Dropping out of school
Epidemiology and race

- Black youth have lower rates of substance use than Whites or Hispanics
- Blacks and Hispanics
  - Less likely to drink
  - More likely to have chronic dependence once disorder develops
- Hispanic girls have lower rates of alcohol consumption
  - May mask severity of Hispanic male consumption

Predictive factors

- Factors
  - Age of first use
    - 40% of children who begin drinking before age 15 will develop alcohol dependence
  - Developmental level
  - Frequency of use
    - More important than duration of use
- Predicts more rapid progression

Substance abuse and sexual behaviors

- Risk-taking behavior while intoxicated
  - Unprotected sex may lead to pregnancy
- Drug use causes irregular menstrual cycles, but can still conceive
  - May not realize she is pregnant for several months
Opioids: Effects on fetus

- No known fetal anomalies
- Intrauterine growth retardation
- Neonatal abstinence syndrome
  - Continuous exposure
  - Use up to delivery

Smoking: Effects on fetus

- Most common fetal exposure
- Intrauterine growth retardation
- Higher rates of spontaneous abortion, placenta previa, etc.
- SIDS risk >4x higher
- Nicotine patch better than smoking cigarettes

Alcohol: Effects on fetus

- Fetal Alcohol Syndrome
- Fetal Alcohol Effects
- Spectrum disorder
- Leading preventable cause of mental retardation
- Encourage abstinence as soon as pregnancy suspected
Medication-Assisted Therapy

- **Opioids**
  - Prescription painkillers
  - Heroin
- **Tobacco**
  - Cigarettes
  - Smokeless tobacco
  - Electronic cigarettes
- **Alcohol**
  - Beer
  - Wine
  - Liquor

Opioid addiction treatments

- Abstinence-based
  - Narcotics Anonymous
  - Residential (with or after detox)
- Behavioral
  - Motivational Interviewing
  - Cognitive-behavioral (CBT)
- Antagonist maintenance
  - Naltrexone
- Opioid maintenance
  - Methadone
  - Buprenorphine

Nicotine Pharmacotherapy

- Replacement
  - nicotine patches
  - nicotine gum
  - nicotine nasal spray
  - lobeline (CigArrest)
- Partial agonists
  - Varenicline (Chantix)
- Antidepressants
  - Bupropion (Zyban)
  - Fluoxetine (Prozac)
- Antagonists
  - mecamylamine
- Deterrent therapy
  - silver acetate
Medications for Alcohol Use Disorder

- Acamprosate (Campral)
- Naltrexone
  - Oral (ReVia)
  - Injection (Vivitrol)
- Disulfiram (Antabuse)

Barriers to medication-assisted treatment in adolescents

- Philosophical opposition
- Compliance issues with medication
  - Irresponsibility
  - Cost
  - Interactions
- Denial of severity
  - Both adolescent & family

Coming off

- Plan ahead
- Support system in place
- Communication between counselor and client
  - Meeting treatment goals
  - Achieved stability
  - Relapse risk factors
- Taper down slowly to avoid withdrawal
- Transition to treatment without pharmacotherapy
  - Treatment doesn’t end, just medication prescription
Monitoring for relapse

- Patient report
- Clinical observation
- Collateral information
  - Family
  - Other counselors
  - Probation officer
- Urine drug screening

Relapse: What to look for

- Evasive behavior
- Missing sessions
- Worsening of personal hygiene
- Appears intoxicated
- Hang out with friends who use
- Legal problems
- Reversal of sleep-wake cycle (staying up all night)

Relapse: What to do

- Relapses and remissions are part of any chronic disease process
- Intensify treatment efforts
- Safety issues
  - Overdose risk
- Permission to communicate with others
Questions?

Lunch Time!

Pharmacotherapy for Opioid Use Disorder
Antagonists vs Agonists

- Opioid Antagonists
  - Naloxone (Narcan)
    - Overdose treatment
    - IV, nasal spray
    - Works rapidly
    - Wears off quickly
  - Naltrexone
    - Oral or intramuscular
    - Long-term pharmacotherapy
    - Take regularly for maintenance treatment

- Opioid Agonists
  - Methadone
    - For addiction treatment, restricted to licensed treatment programs
    - Also prescribed for chronic pain management
  - Buprenorphine
    - Office-based opioid treatment (OBOT)
    - Multiple brand names

Naltrexone

- Blocks opioid receptors
  - No effect from using
- Reduces cravings
- Available as
  - Tablets taken daily
  - Intramuscular injection given monthly
- Must be taken to be effective
  - Best when monitored
  - Motivation is key

Oral naltrexone (ReVia)

- Once-daily tablet
- Tablets are much less expensive than injection
  - Generic form available
  - Covered by health insurance
- Requires motivation to take every day
  - Not providing a positive, but preventing a negative
  - Less effective when doses are missed
- No street value
Injectable naltrexone (Vivitrol)

- Intramuscular injection of depot naltrexone given monthly
- Administer in physician office, not at home
- Requires patient motivation
- Advantages of injection
  - Better compliance
  - Less potential for liver toxicity

Naltrexone for Opioid Use Disorder

- Reasonable alternative to opioid agonist maintenance
- May be better for
  - Motivated patients
  - Not using high doses of opioids
  - Concern about diversion
  - Adolescents

Short-term detoxification

- Agonist medication given for <180 days
- Stabilization of withdrawal symptoms and behavior over weeks/months
- Taper over a few months
- Option for those who don’t meet criteria for maintenance
- Risk of overdose after tapering off
Opioid Agonist Maintenance

- Long-term pharmacotherapy
- Allows time for full stabilization
  - Establishment of recovery support system
  - Coping skills
  - Employment
  - Stable housing
  - Parenting skills
  - Citizenship
- Indefinite endpoint
- Longer time using often means longer time for full stabilization
- May take a long time to “unlearn” addictive behaviors and work on coping skills
- Months to years
  - Not usually lifelong

Methadone

- Opioid substitution therapy
- Long-acting medication in controlled setting
  - Counseling
  - Social services
- Avoid withdrawal & craving
- Harm reduction
  - Individual
  - Society

Methadone Maintenance

- Use of methadone for >180 days (6 mo.)
- Single daily observed dose
- Highly regulated
  - Narcotic treatment programs must be licensed
- Referral for primary medical services
Methadone

- Long-acting pure opioid agonist
- Requires daily clinic visits, but may get take-home dose privileges
- Significant street reputation
- Also used for pain like other Schedule II opioids

Requirements

- Physical dependence
  - At least 1 year of use
    - Continuous
    - Intermittent
  - Withdrawal signs
- Not physically dependent if just released from
  - Incarceration
  - Hospital
- 18 years old or older

Efficacy of methadone

- There have been many studies and several meta-analyses
- Maintenance superior to detox
- Higher doses (80-100 mg/day) superior to lower doses (50 mg/d)
  - ↓ illicit opioid use
  - ↑ retention in treatment
- Decreases criminal activity
- Reduces spread of HIV
- Results similar to long-term therapy of most chronic diseases
Does methadone get you high?

- No real euphoria
  - Onset latency
- Does cause sedation
  - Typical opioid effects
  - Reassuring
  - Confused with “high”
- Mix with other drugs
  - benzodiazepines

Methadone and Pregnancy

- Standard of care for opioid-dependent pregnant women
- Stabilization of mother and fetus
  - Medical and social
  - Higher dose in 3rd trimester
  - Improves growth of fetus & newborn
  - Decreases practice of high-risk behaviors

Methadone forever?

- No specific limit for time on methadone
  - Some states restrict time
- Individual variability
  - Time required to stabilize (drug use, housing, family, job)
  - Long-term clients
- Initial: can’t imagine life without *something*
- Stable: able to consider coming off
  - Taper off comfortably over months/years
Buprenorphine

- Alternative to methadone for opioid addiction treatment
- Multiple forms available
  - Combined with naloxone (Suboxone, Zubsolv, Bunavail)
  - Buprenorphine only (Subutex)
- Detox or maintenance
- Long-acting opioid agonist-antagonist

Buprenorphine is an agonist-antagonist

- Binds to opioid receptors in body
- Only activates receptor around 40%, not 100% like other opioids (heroin, methadone)
  - If already in withdrawal, 40% is pretty good
  - If not in withdrawal, dropping from 100% to 40% receptor activation causes withdrawal
- Very low risk of overdose
  - Can OD when combined with sedative (benzos)

Buprenorphine/naloxone

- Combination helps reduce abuse
- Naloxone only active when Suboxone is injected
- Results in withdrawal for users trying to get high
- Buprenorphine alone has similar effect when injected by those who are opioid dependent and not in withdrawal already
What is the right dose?

- Individually determined
  - Based on tolerance, withdrawal
  - Other medications, physical activity level
- Most patients on 12-16 mg daily
  - Over 32 mg/day is less well tolerated

Office-based opioid therapy

- Buprenorphine is less restricted than methadone (Schedule III)
  - Get prescription from pharmacy with refills (up to 6 months)
  - Outpatient physician visits for medication checks as needed
- Addiction counseling is separate, patient may be referred to another provider for this service

Adolescents

- Buprenorphine less age-restricted
  - Can use at age 16
  - Methadone limited to age 18
  - Niche for adolescents who don’t qualify for methadone due to age
Study of buprenorphine treatment in adolescents

- Multi-center trial
- Funded by NIDA
- Compared short detox (2 weeks) to maintenance (12 weeks)
- Age 14-21 years old
- Required weekly CBT counseling
- Maintenance group did better
  - Fewer opioid(+) urines
  - Attended more counseling sessions
  - Better retention in treatment
- Detox group used more cocaine and marijuana, and injected more

Buprenorphine and Pregnancy

- Pregnancy Category C
- Use Subutex instead of Suboxone to avoid naloxone
- NAS less intense than with methadone
- Studies ongoing, results encouraging

Referral for treatment

- Opioid dependence
- Available in area
- Ability to afford
- Ability to adhere
- Diversion risk
- Contraindications
- Website: findtreatment.SAMHSA.gov
- Provider locator
- Information for patients and providers
Summary

- Naltrexone helps prevent relapse after detox
- Substitution therapy eliminates withdrawal, cravings, & heroin effects
- Maintenance treatment has been proven to reduce mortality, crime, & spread of infection
- Buprenorphine is less restricted than methadone
- Use buprenorphine for age 16 and up
- Individualized dose and time on maintenance

Questions?

First Case for Group Discussion
Case #1
- 16 y/o White male
- First tried heroin at age 14
- Snorts $60 of heroin daily for past 10 months
- Longest abstinence: 2 weeks
- Also smokes marijuana, drinks 2-3 beers most weeknights, more on weekends

Case questions
- What type of treatment offers the best chance to prevent relapse?
- Is there any pharmacotherapy that is unavailable to this patient currently?
- In addition to treatment for opioid use disorder, what other issues need to be addressed?

Cases for Group Discussion
Pharmacotherapy for Tobacco Use Disorder

Nicotine Withdrawal
- craving for tobacco
- irritability, frustration, anger
- anxiety
- difficulty concentrating
- restlessness
- decreased heart rate
- increased appetite or weight gain
- depression
- disrupted sleep
- sedation

Nicotine Withdrawal
- Begins within 24 hours of last cigarette
- Lasts 2 - 4 weeks
- Tobacco craving & increased hunger may last for 6 months or more
Nicotine replacement therapy
- Always combine with a behavioral therapy program
- Most available OTC
- Reduces harmful effects of tobacco smoking
- Patients should not smoke while using

Nicotine Patch
- Highest success rate of available nicotine replacement pharmacotherapies
- Nicoderm, Nicotrol, Habitrol, Prostep
- Most come in 3 strengths: 21, 14, & 7mg
- Start with 21mg patch for 6 wks, taper to 14 mg for 2 wks, finally 7 mg for 2 weeks
- Use new patch in different spot on upper trunk every 24 hrs

Nicotine Gum
- Nicorette - 2 or 4mg per piece doses
- Requires correct “chewing technique” -- don’t chew like regular chewing gum
- Chew 1 piece for 30 minutes every 1 to 2 hours to prevent nicotine withdrawal
- Chew regularly for first month, then taper off over 6 months
Nicotine Nasal Spray

- Reduces nicotine craving & mimics pleasurable effects of nicotine
- 1 spray in each nostril, up to 40 times in 24 hours
- Use for up to 3 months
- May cause tearing, sneezing, & burning sensation in nose

Bupropion (Zyban)

- Bupropion 150mg sustained release pills
- Works on dopamine & norepinephrine receptors in the brain to decrease withdrawal
- May cause insomnia, anxiety, or seizures
- Prescription includes behavioral program
- Start pills 10-14 days before "quit date"
- Take daily for 3 days, then twice a day
- Continue pills for 8 - 12 weeks

Varenicline (Chantix)

- Nicotine partial agonist
- Start pills 10 days before quit date
  - Increase dose
  - Take for 12-24 weeks
- Includes behavioral program
Efficacy of tobacco cessation products

- There have been many studies and several meta-analyses of all products
- Nicotine replacement therapy quit rates are similar with different products
  - Doubles chance of successful quitting
- Combinations are more effective than a single product at a time

Varenicline
- Higher rate of continuous tobacco abstinence compared to bupropion & nicotine patch

Bupropion
- Quit rates are comparable to nicotine patch

What patients can expect when quitting smoking

- Temporary increase in cough
- Weight gain
- Nicotine withdrawal symptoms
- Pressure from other smokers (esp. if family)

Patient Information

- American Cancer Society
- American Lung Association
- American Heart Association
- U.S. Department of Health & Human Services
Questions?

Break Time

Please return in 15 minutes to begin small group case discussions for Tobacco Use Disorder

Cases for Group Discussion
Pharmacotherapy for Alcohol Use Disorder

- Acamprosate (Campral)
- Naltrexone (ReVia, Vivitrol)
- Disulfiram (Antabuse)

Acamprosate (Campral)

- Alcohol use disorder pharmacotherapy
- No drug interactions
- Minimal side effects
  - Diarrhea
- Does not treat withdrawal symptoms
- Reduces symptoms of protracted abstinence
  - Insomnia
  - Anxiety
  - Restlessness
- Treat for 12 months
  - Effect sustained for at least 12 months more

Acamprosate in Adolescents

- Limited clinical data on use in adolescents
- Randomized study of 26 subjects age 16-19 with chronic or episodic alcohol use
  - Acamprosate or placebo for 90 days
  - Greater abstinence on acamprosate
- Advantages over disulfiram
  - Well-tolerated
  - No drug interactions
Naltrexone (ReVia)

- Once-daily tablet
- Blocks opioid receptors
  - Reduces pleasurable effects of alcohol
- Reduce craving
- Reduces alcohol slips
  - Prevents escalation to full-blown relapse
- Used for opioids as well as alcohol

Oral naltrexone in Adolescents

- Safe and well-tolerated in open-label trial of 5 adolescents
  - Reduced alcohol consumption and craving
- Randomized trial of 128 subjects age 18-25
  - Reduced drinking intensity (fewer drinks per day)
  - Did not reduce frequency of drinking

Injectable naltrexone (Vivitrol)

- Intramuscular injection of depot naltrexone given monthly
- FDA approved for alcohol and opioids
- Administer in physician office, not at home
- Requires patient motivation
Disulfiram (Antabuse)

- Blocks acetaldehyde dehydrogenase
- Reaction to alcohol
  - Flushing, palpitations, chest tightness
  - Nausea, headache, anxiety
- Avoid slips or relapses
- Affects liver, even without alcohol
- Motivation is necessary
  - Monitored dosing

Disulfiram in Adolescents

- Use in adolescents not formally approved
- Efficacy and side effect information is extrapolated from adult data
- Randomized study of 26 subjects age 16-19 with chronic or episodic alcohol use
  - Greater abstinence on disulfiram
  - No difference in side effects
- Not a preferred agent for adolescents

Efficacy of AUD pharmacotherapy

- There have been many studies and several meta-analyses of all products
- Naltrexone
  - Injection: ↓ drinking by 25% more than placebo
  - Pills: ↓ risk of heavy drinking by 17% more than placebo
- Acamprosate
  - ↓ drinking by 14% more than placebo
  - Better for maintenance of abstinence than initiation if not abstinent
- Disulfiram
  - Longer time to 1st drink compared to other meds
  - Reduced overall drinking
  - Only when monitored
    - Less benefit when not monitored
Questions?

Cases for Group Discussion

Thank you!

Michael Weaver, MD