

# Pharmacotherapy in the Treatment of Alcohol Use Disorders

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# Medication Used to Treat AUD

- Detoxification agents
- Medications used to reduce or stop drinking

# Neurophysiology of Alcohol Withdrawal

- In response to alcohol's depressant effects, body adjusts in order to maintain homeostasis
  - "Downregulation" of inhibitory systems
  - "Upregulation" of excitatory systems
- Cessation of alcohol use "unmasks" these changes



# Alcohol Withdrawal Symptoms

- Craving
- Tremor
- Anxiety
- Sweating
- Insomnia
- Nausea
- Rapid pulse
- ↑ Blood pressure
- Fever
- DTs
- Seizures

# Medications Used for Detoxification

- Some patients with AUD do not need medical detoxification
- Those who do have worse withdrawal symptoms
- For more severe withdrawal:
  - Benzodiazepines
    - Those with longer half-life preferred (Librium, Valium)
  - Phenobarbital (Less common)

# Medications used to reduce or stop drinking

- Disulfiram (Antabuse)
- Naltrexone
- Acamprosate
- Anticonvulsants
- Baclofen



# Alcohol's Metabolic Pathway

ALCOHOL

Alcohol dehydrogenase

ACETALDEHYDE

Aldehyde dehydrogenase

ACETIC ACID

CO<sub>2</sub> AND H<sub>2</sub>O

# Disulfiram

- Blocks the conversion of acetaldehyde to acetic acid
- Inhibits aldehyde dehydrogenase
- Drinking produces aversive effects (disulfiram-ethanol reaction/DER)
  - Flushing
  - Dizziness
  - Sweating
  - ↓ blood pressure
  - Nausea and vomiting



# Disulfiram

- Drinking produces aversive effects
  - Blurred vision
  - Confusion
  - More rarely/high doses of Antabuse and alcohol
    - Extremely rapid or slowed heart rate
    - More extreme ↓ blood pressure
    - Cardiovascular collapse
    - Congestive failure
    - Convulsions

# Disulfiram

- Most reactions last about 30 minutes
- Efficacy depends on patient compliance
- May limit length of relapse
- Lack of methodologically sound evidence that Antabuse prevents relapse
- Lack of guidelines for which psychosocial interventions are best suited to enhance compliance

# Disulfiram

- Patients need to be monitored for:
  - Optic neuritis
  - Peripheral neuropathy
  - Hepatotoxicity



# Naltrexone (ReVia)

- Well tolerated physically
- Alcohol detox must be completed
- An opioid antagonist

# Naltrexone (ReVia)

- Alcohol works in part through the endogenous opioid system
- Makes drinking less pleasurable
- Evidence suggests that naltrexone reduces craving for alcohol, drinking days and length of relapse Vs. placebo

# Naltrexone (ReVia)

- Depot form (intramuscular injection) works for 30 days
- Research suggests that naltrexone combined with psychosocial interventions (e.g., coping skills) works better than naltrexone alone
  - CBT
  - MET
  - 12-Step Facilitation



# Acamprosate

- An amino acid derivative that both increases GABA (gamma aminobutyric acid) and decreases glutamate
- Latter thought to be basis for effects on AUD
- Also increases  $\beta$ -endorphins
- Rare side effects are generally mild and transient
  - Diarrhea, bloating
  - Pruritus
- May work better in combination with disulfiram

# Acamprosate and Naltrexone

- No contraindications against combining
- Studies vary in their outcomes, but no clear advantage to combination found except Vs. placebo
- Psychosocial interventions an advantage

# Anticonvulsants

- Topiramate
- Carbamazepine
- Reduces glutamate levels
- Some studies have found carbamazepine superior to placebo in reducing:
  - Time to first heavy drinking day
  - Drinks per drinking day
  - Number of consecutive drinking days
- Similar results with other anticonvulsants
- Not FDA-approved for treatment of AUD



# Baclofen

- Muscle relaxant/antispasmodic
- Acts as GABA-B agonist
- Good safety profile for those with liver disease
- Inconsistent research results
  - Time to relapse
  - Decrease in alcohol intake
  - Abstinence
- Not FDA-approved for treatment of AUD

# Treating Co-Occurring Psychiatric Disorders

- Subacute withdrawal (alcohol PAWS)
  - Anxiety
  - Depression
- Clinicians must differentiate subacute withdrawal from diagnosable psych disorders
- Antidepressants, lithium, antipsychotics and benzodiazepines have been used to treat co-occurring AUD and other psych diagnoses
- MD's must be careful to avoid contraindications, potentially bad cross-reactions and BUD



THANK YOU FOR YOUR ATTENTION!

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