Alcohol Withdrawal

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Learning Goals/Objectives

- **Discuss the diagnosis of and screening for alcohol use disorder and alcohol withdrawal**
- **Recognize the time course of alcohol withdrawal symptoms**
- **Learn the different strategies involved in medicating patients presenting with alcohol withdrawal**
- **Discuss some medications approved for the treatment of alcohol use disorder**

Standard Drink Definitions

- A standard drink is defined as approximately 14 g of absolute ethanol, or 0.6 fluid ounces
  - 12 ounces of beer (5%)
  - 5 ounces of wine (12%)
  - 1.5 ounces of liquor (40% or 80 proof)
- Keep in mind that not all beers, wines, and liquors are the same- craft beers, malt liquor, fortified wines, and higher proof liquor
- Also keep in mind the size of the container- 40 ounce beers, pint draughts, etc.

How much is too much?

- The National Institute of Alcohol Abuse and Alcoholism of the National Institutes of Health (NIAAA) recommends:
  - Men: No more than 4 drinks per day and 14 drinks per week
  - Women and those over 65: No more than 3 drinks per day and 7 drinks per week
- Drinking within these limits is considered "low-risk" drinking
  - Conversely, drinking more than this on a regular basis is termed "heavy drinking"
  - "At-risk drinking": heavy drinking in the absence of alcohol use disorder
- Lower limits or abstinence may be indicated in the presence of coexisting medical or psychiatric disorders, when medication interactions are a concern, or with a safety-sensitive job
- Women who are pregnant or at risk of becoming pregnant are advised to abstain, as should alcoholics and children/adolescents

Epidemiology

- 12-month prevalence of alcohol use disorder
  - 12-17 year olds- 4.6%
  - 18 and older- 8.5%
    - Adult Men- 12.4%
    - Adult Women-4.9%
- Most studies have found that the prevalence of alcohol use disorders is highest among young adults (18-29 years old)
- Approximately half of the US population report current drinking (having at least 1 drink in the prior month)
- In the most recent survey (2011 National Survey on Drug Use and Health):
  - 22.6% reported binge alcohol use (5 or more drinks on at least one occasion in the last month)
  - 6.2% reported heavy drinking (binge drinking 5 or more days in the last month)

DSM-5 Alcohol-Related Disorders

- Alcohol use disorder
  - Mild
  - Moderate
  - Severe
- Alcohol Intoxication
- Alcohol Intoxication Delirium
- Alcohol Withdrawal
- Alcohol Withdrawal Delirium
- Unspecified Alcohol-Related Disorder
- Alcohol-induced
  - Major neurocognitive disorder
  - Minor neurocognitive disorder
  - Psychotic disorder
  - Bipolar disorder
  - Depressive disorder
  - Anxiety disorder
  - Sexual dysfunction
  - Sleep disorder

DSM-5 Changes to Substance Use Disorders

- Change in terminology- no longer abuse and dependence
  - Dependence is a misunderstood term that has negative connotations when in fact it is a physiologic phenomenon that can occur with proper use of medications
  - Further, studies indicate that DSM-IV substance abuse and substance dependence criteria represent a singular disorder with differing levels of severity

Substance Use Disorder Diagnosis

- Now, 11 criteria in DSM-5
  - 4 abuse criteria, plus
  - 7 dependence criteria, plus
  - Craving or strong desire/urge to use, minus
  - Legal consequences
- Why add craving criteria?
  - Highly validated, based on clinical trials and brain imaging data, and may hold potential as a future biomarker for the diagnosis of SUD
- Why subtract legal consequences?
  - It has poor clinical utility and its relevance to patients varies based on local laws and enforcement of those laws

Diagnosis of Alcohol Use Disorder in DSM-5

A. A problematic pattern of alcohol use leading to clinically significant impairment or distress, as manifested by at least two of the following, occurring within a 12-month period:
   1. Alcohol is often taken in larger amounts or over a longer period than was intended.
   2. There is a persistent desire or unsuccessful efforts to cut down or control alcohol use.
   3. A great deal of time is spent in activities necessary to obtain alcohol, use alcohol, or recover from its effects.
   4. Craving, or a strong desire or urge to use alcohol.

DSM-5 Criteria for Alcohol Use Disorder (continued)

5. Recurrent alcohol use resulting in a failure to fulfill major role obligations at work, school, or home.
6. Continued alcohol use despite having persistent or recurrent social or interpersonal problems caused or exacerbated by the effects of alcohol.
7. Important social, occupational, or recreational activities are given up or reduced because of alcohol use.
8. Recurrent alcohol use in situations in which it is physically hazardous.
9. Alcohol use is continued despite knowledge of having a persistent or recurrent physical or psychological problem that is likely to have been caused or exacerbated by alcohol.

DSM-5 Criteria for Alcohol Use Disorder (continued)

10. Tolerance, as defined by either of the following:
    a. A need for markedly increased amounts of alcohol to achieve intoxication or desired effect.
    b. A markedly diminished effect with continued use of the same amount of alcohol.
11. Withdrawal, as manifested by either of the following:
    a. The characteristic withdrawal syndrome for alcohol (refer to criteria set for alcohol withdrawal).
    b. Alcohol (or a closely related substance, such as a benzodiazepine) is taken to relieve or avoid withdrawal symptoms.

Core Features of Alcohol Use Disorder

- Criteria are grouped according to similar symptoms:
  - Criteria 1-4: Impaired control
  - Criteria 5-7: Social impairment
  - Criteria 8-9: Risky use
  - Criteria 10-11: Pharmacological criteria
- Criteria does not include parameters regarding amount, frequency, or pattern of use

DSM-5 Specifiers for Alcohol Use Disorder

- Specify current severity
  - Mild- presence of 2-3 symptoms
  - Moderate- presence of 4-5 symptoms
  - Severe- presence of 6 or more symptoms
- Other Specifiers
  - In early remission (3-12 months w/o symptoms)
  - In sustained remission (more than 12 months)
  - In a controlled environment

Screening for Substance Use

- Ask your patients about their substance use:
  - How many alcoholic drinks do you have in a week?

    (not: "Do you drink alcohol?")
  - Ask about nicotine and each of the common illicit drugs specifically.
- Try to start with the least charged topics first to get them more comfortable
- Discuss without criticism or judgment
- Follow up on positive responses

Screening Tools for Alcohol Use Disorder

- CAGE questionnaire
  - C-Have you ever felt you ought to CUT DOWN your drinking?
  - A-Have people ANNOYED you by criticizing your drinking?
  - G-Have you ever felt GUILTY about your drinking?
  - E-Have you ever had a drink first thing in the morning (EYE OPENER) to steady your nerves or get rid of a hangover?
- Two or more "yes" responses is a positive screen

Other Tools Available

- Multiple more detailed screens available
  - Alcohol Use Disorders Identification Test (AUDIT/AUDIT-C)
  - Michigan Alcohol Screening Test (MAST)
- Consider using point-of-care testing
  - Breathalyzer
  - Saliva or urine testing for alcohol

DSM-5 Criteria for Alcohol Withdrawal

A. Cessation of (or reduction in) alcohol use that has been heavy and prolonged.
B. Two (or more) of the following, developing within several hours to a few days after the cessation of (or reduction in) alcohol use described in Criterion A:
   1. Autonomic hyperactivity (e.g., sweating or pulse rate greater than 100 bpm).
   2. Increased hand tremor.
   3. Insomnia.
   4. Nausea or vomiting.
   5. Transient visual, tactile, or auditory hallucinations or illusions.
   6. Psychomotor agitation.
   7. Anxiety.
   8. Generalized tonic-clonic seizures.

DSM-5 Criteria for Alcohol Withdrawal (continued)

C. The signs or symptoms in Criterion B cause clinically significant distress or impairment in social, occupational, or other important areas of functioning.
D. The signs or symptoms are not attributable to another medical condition and are not better explained by another mental disorder, including intoxication or withdrawal from another substance.

Specify if: With perceptual disturbances

Rate of Alcohol Metabolism

- **Metabolism:**
  - **For a person with an average rate of alcohol metabolism, the blood alcohol level would drop by 0.010-0.020 g/dL per hour.**
- **A patient with alcohol use disorder may begin to show alcohol withdrawal with a blood alcohol content (BAC) well above the "legal limit" (0.080 g/dL in those over age 21)**
  - **Example: A patient admitted to the hospital with BAC 0.400 may begin to have withdrawal symptoms 10 hours after arrival**
  - **BAC ~0.200 when withdrawal begins**

Pathophysiology of Alcohol Withdrawal

- **Alcohol produces CNS depression via GABAergic neurotransmission**
- **GABA = inhibitory**
  Glutamate = excitatory
- **Cessation of alcohol = removal of GABA activity = removal of inhibition= results in excitatory state**
- **Thus, the withdrawal symptoms exhibited are a result of this excitatory state**

Approach to the Patient in Alcohol Withdrawal

- Comprehensive history and physical
- Routine lab tests
  - Alcohol level
  - CBC with differential and platelets
  - Chemistry, including Mg, Ca, and Phos
  - LFTs
  - PT/INR
  - Comprehensive drug screen
  - Pregnancy test in females
- Consider
  - Lipase
  - Uric acid
  - Ammonia
  - Volatile alcohol panel
  - TB skin test
  - Chest X-Ray
  - EKG or Telemetry for underlying cardiac disease
  - Testing for hepatitis and STDs

Appropriate Treatment Setting

- Disposition is determined by the patient's stage of withdrawal and history of complicated withdrawals

Outpatient	Mild symptoms, no history of complicated withdrawal, no significant medical or psychiatric problems; should be seen daily if possible with a responsible person available to monitor at home; can use loading dose or fixed dose tapers
Inpatient detox	Depends on detox facility; usually requires management with PO benzos; a history of complicated withdrawals (including delirium or seizures)
Inpatient medical hospital	Requires IV benzos for treatment; comorbid medical illness requiring medical admission; medical admissions often precipitate alcohol withdrawal; recommend screening of all admitted patients
Medical ICU	Delirium tremens; high-dose IV benzos requiring benzo drip

Timeline of Alcohol Withdrawal Symptoms

Stage	Onset (hours since last drink)
Withdrawal symptoms	6-36 hours
Hallucinosis	12-48 hours
Alcohol-withdrawal seizures	8-48 hours
Alcohol Withdrawal Delirium/ Delirium tremens	48-96 hours

- **Not everyone will progress through each stage**
- **Do not need to experience one step to progress to the next**
- **For example, can experience delirium tremens without having seizures or hallucinosis**

Alcohol Withdrawal Hallucinosis

- **~25% of patients develop perceptual symptoms**
- **Develop 12-48 hours after last drink**
- **Usually visual hallucinations, may also be auditory or tactile**
- **Patient recognizes symptoms as unreal**
- **Differentiated from delirium tremens by the presence of intact sensorium**
- **Usually resolve within 48 hours**

Alcohol Withdrawal Seizures

- Generalized tonic-clonic seizures that usually occur 8-48 hours from last drink, peaks at 24 hours
  - However, can occur as early as 2 hours after last drink
- Typically short or no post-ictal period
- Risk of seizures increases with repeated withdrawal
  - Kindling- an individual with previous alcohol withdrawal may be more likely to have more complicated withdrawal in future episodes; thought to be due to neuronal excitability and sensitivity that develops during alcohol withdrawal
- Approximately 3% of alcohol withdrawal seizures progress to status epilepticus
  - Risk increases if also withdrawing from sedative-hypnotics

Alcohol Withdrawal Delirium "Delirium Tremens"

» Hallmark of DT's is Delirium:
  » Altered level of consciousness
  » Disorientation
  » Confusion
  » Vivid visual hallucinations without insight
» Autonomic storm- fever, tachycardia, hypertension
» Gross tremor
» Psychomotor agitation
» Sleep/wake disruption

Alcohol Withdrawal Delirium

- Occurs in 5% of patients with alcohol withdrawal
- Mortality risk 1-5% (10-20% if left untreated)
  - Alcohol withdrawal can be a life threatening condition
  - Remember life-threatening withdrawals- alcohol, benzodiazepines, and barbiturates
- Timing:
  - Onset usually 48-96 hours after last drink, but can begin up to 10 days after last drink
  - Typical duration 2-3 days but can last 7 or more

Predictors of Severe Alcohol Withdrawal

- High CIWA scores early in treatment course/despite BAL
- Previous DT's or withdrawal seizures
- Marked autonomic hyperactivity
- BAL > 0.100 g/dL on admission
- Serum electrolyte abnormalities
- Sustained heavy drinking
- Concurrent medical illness
- Longer delay before presenting for treatment of withdrawal
- Age >30

Measuring Alcohol Withdrawal

- Best studied scale is the CIWA-Ar
  - Clinical Institute Withdrawal Assessment for Alcohol – revised
- Useful assessment of subjective symptoms of alcohol withdrawal: 10 symptom categories
- Does not include measurement of vital sign abnormalities
- However, symptoms can be over-reported (anxiety, sensory symptoms, headache) resulting in over-use of benzodiazepines
- Maximum score of 67
  - ≤ 9 = mild withdrawal
  - 10-18 = moderate withdrawal
  - > 18 = severe withdrawal

CIWA-Ar

Nausea/vomiting (0 - 7)
- 0 - none; 1 - mild nausea, no vomiting; 4 - intermittent nausea; 7 - constant nausea , frequent dry heaves & vomiting.

Tremors (0 - 7)
- 0 - no tremor; 1 - not visible but can be felt; 4 - moderate w/ arms extended; 7 - severe, even w/ arms not extended.

Anxiety (0 - 7)
- 0 - none, at ease; 1 - mildly anxious; 4 - moderately anxious or guarded; 7 - equivalent to acute panic state

Agitation (0 - 7)
- 0 - normal activity; 1 - somewhat normal activity; 4 – moderately fidgety/restless; 7 - paces or constantly thrashes about

Paroxysmal Sweats (0 - 7)
- 0 - no sweats; 1 - barely perceptible sweating, palms moist; 4 - beads of sweat obvious on forehead; 7 - drenching sweat

Orientation (0 - 4)
- 0 - oriented; 1 - uncertain about date; 2 - disoriented to date by no more than 2 days; 3 - disoriented to date by > 2 days; 4 - disoriented to place and/or person

CIWA-Ar

Tactile Disturbances (0 - 7)
- **0 - none; 1 - very mild itch, P&N, numbness; 2-mild itch, P&N, burning, numbness; 3 - moderate itch, P&N, burning ,numbness; 4 – moderate hallucinations; 5 - severe hallucinations; 6 – extremely severe hallucinations; 7 - continuous hallucinations**

Auditory Disturbances (0 - 7)
- **0 - not present; 1 - very mild harshness/ ability to startle; 2 – mild harshness, ability to startle; 3 - moderate harshness, ability to startle; 4 - moderate hallucinations; 5 severe hallucinations; 6 - extremely severe hallucinations; 7 - continuous.hallucinations**

Visual Disturbances (0 - 7)
- **0 - not present; 1 - very mild sensitivity; 2 - mild sensitivity; 3 - moderate sensitivity; 4 - moderate hallucinations; 5 – severe hallucinations; 6 - extremely severe hallucinations; 7 - continuous hallucinations**

Headache (0 - 7)
- **0 - not present; 1 - very mild; 2 - mild; 3 - moderate; 4 – moderately severe; 5 - severe; 6 - very severe; 7 - extremely severe**

Keep in mind

- **The CIWA-Ar takes 2-5 minutes to complete**
- **Has proved useful in a variety of settings, including detoxification units, psychiatric units, med/surg units, ICU's**
- **Important that all staff be sufficiently trained on its use to reduce interobserver variability**
- **Beware of the intoxicated patient with non-specific symptoms, or comorbid medical conditions or medications increasing or decreasing scores**
- **CIWA is not a diagnostic instrument- helps to determine severity and monitor course**

Pharmacologic Treatment of Alcohol Withdrawal

- Gold standard of treatment = benzodiazepines
- Longer acting agents are most commonly used:
  - Chlordiazepoxide
  - Diazepam
  - Lorazepam – does not require metabolism by hepatic oxidation and is preferred for patients with hepatic dysfunction
    - Remember LOT- also oxazepam and temazepam
  - AVOID short acting agents (alprazolam)
- Phenobarbital- sometimes used in place of benzodiazepines in patients with severe withdrawal symptoms

Further Considerations

- Keep in mind time of onset and half-life of medication you are using
- Benzodiazepines should be given PO or IV for reliable absorption
  - Exception- lorazepam has reliable absorption IM and SL
- Clinical status of patient often determines choice of medication
  - Not all benzos available IV
  - Hepatic impairment
- Recommend becoming very familiar with 1-2 agents that you consistently use

Dosing Regimens for Alcohol Withdrawal

- Symptom-triggered therapy
  - Example: Diazepam 5-20mg with range based on CIWA score
  - Repeat monitoring every hour initially, then every 4 hours until CIWA score below 8-10 for 24 hours
  - Often preferred by programs specializing in the management of addiction
- Fixed-dose taper
  - Example: Diazepam 10-15mg QID x 1 day, then TID x 1 day, then BID x 1 day, then daily x 1 day
  - May be more appropriate in general med/surg wards with less experienced staff
  - Can also combine fixed-dose taper with additional symptom-triggered therapy
  - Make sure there are hold parameters for over-sedation

Dosing Regimens for Alcohol Withdrawal

- Loading dose
  - Diazepam 10-20mg IV q1h until symptoms diminish
  - Drug self-tapers due to long half-life
  - Sometimes requires additional load within the first 24 hours

Additional Medications for Alcohol Withdrawal

- Flumazenil as needed for benzodiazepine overdose
- Thiamine 100 mg PO/IM/IV daily x 3 days
  - To help prevent Wernicke-Korsakoff syndrome
  - Can be given TID or up to 500 mg daily if treating Wernicke-Korsakoff
- Folic acid 1 mg daily
- Multivitamin daily
- Replace electrolytes, especially potassium and magnesium
- Consider IV hydration (D5NS)
  - Always give thiamine prior to glucose

After Acute Withdrawal

- Referral to treatment
  - Detox alone is likely not enough
  - Many treatment settings available
    - Residential treatment, partial hospitalization, intensive outpatient programs, outpatient counseling
- Learn the resources available in your area
- For many patients, Alcoholic Anonymous can provide a support system
  - However, not a substitute for treatment

Medications for Alcohol Use Disorder

Medication	Brand Name	Dose	Mechanism	Other Facts
Disulfiram	Antabuse	250 mg daily	Aversive symptoms if alcohol ingested	Risk of death if alcohol ingested; less use now with newer options
Naltrexone (oral)	Revia	50 mg daily	Opioid antagonist	Decreases reinforcing effects of alcohol; monitor hepatic function
Acamprosate	Campral	666 mg TID	GABA agonist & NMDA modulator	Most robust effect is to maintain abstinence; renal excretion
Naltrexone (IM)	Vivitrol	380 mg IM monthly	Opioid antagonist	May help improve adherence; like oral form, reduces risk of heavy drinking

Summary

- **Alcohol withdrawal is a potentially life-threatening condition if left untreated**
- **There are screening tools available to aid in the diagnosis and monitoring of alcohol withdrawal**
- **Alcohol withdrawal syndrome can include hallucinosis, seizures, and delirium**
- **Benzodiazepines are the gold standard for the treatment of alcohol withdrawal**
- **There are several common benzodiazepine dosing regimens, including symptom-triggered dosing, fixed-dose tapers, and loading dose regimens**
- **Following detoxification, patients should be referred to an appropriate treatment facility which can help the patient determine next steps**

Citations

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