How to Diagnose and Treat Alcohol Withdrawal

Learning Objectives:
1) Understand the definition of alcohol withdrawal and recognize its signs and symptoms
2) Describe different approaches in managing alcohol withdrawal

Step 1: Learn the pathophysiology of alcohol withdrawal.

- The primary effects of alcohol on the central nervous system includes enhanced γ-aminobutyric acid (GABA)-ergic and reduced glutamatergic neurotransmission.
- Chronic exposure to alcohol produces adaptive changes in several neurotransmitter systems including GABA, glutamate, and norepinephrine pathways. A down-regulation of $GABA_A$ receptors and upregulation of NMDA glutamate receptors are present. These changes pose targets for treatment of alcohol withdrawal.
- Alcohol withdrawal symptoms typically occur after an abrupt change in regular drinking pattern when alcohol use has been heavy and prolonged. Due to chronic suppression of excitatory neurotransmission via introduction of exogenous GABA (alcohol), after cessation of alcohol consumption relatively increased excitatory neurotransmitter action is present leading to withdrawal symptoms.

Step 2: Recognize signs and symptoms of alcohol withdrawal

- DSM-5 criteria for diagnosis of alcohol withdrawal include two or more of the following symptoms, beginning a few hours or days after stopping or reducing alcohol intake: diaphoresis/tachycardia, hand tremors, difficulty sleeping, nausea/vomiting, illusions or perceptual disturbances, physical agitation, anxiety, seizures.
    - In order to meet DSM-5 criteria for diagnosis of alcohol withdrawal, the above listed symptoms must cause clinical distress or significant impairment in daily functioning and cannot be due to a general medical condition (including withdrawal from other misused substances).
- Components of alcohol withdrawal are listed in Table 1.
- One of the most effective approaches to detect risk of alcohol withdrawal is proactive screening for alcohol use. Two validated screening tools for problematic alcohol use include:
    - AUDIT-C: scores of > 4 for men and > 3 for women are likely indicative of problematic drinking
    - CAGE: score of two positive items indicates a need for further assessment
- Seizures and delirium tremens are considered to be complicated alcohol withdrawal states due to high mortality associated with them.
- Risk factors associated with developing delirium tremens include:
    - History of severe withdrawal symptoms
    - Chronic and significant daily alcohol use
    - Age > 40 years old
    - Multiple medical comorbidities
    - Onset of withdrawal symptoms while having an elevated blood alcohol level

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Table 1: Components of Alcohol Withdrawal

Stages	Findings	Onset
Component 1	Anxiety, agitation, headache, increased heart rate, insomnia, restlessness, tremors	Typically within 12 hours after the last alcoholic drink.
Component 2	Alcohol hallucinosis/ perceptual disturbances including tactile, auditory or visual with intact. Of note, perceptual disturbances can also be seen during alcohol intoxication. Anxiety, agitation, disorientation, paroxysmal sweats, restlessness, tremors may also be present.	Typically within 24 hours after the last alcoholic drink.
Component 3	Alcohol withdrawal seizures	Typically within 48 hours after last alcoholic drink.
Component 4	Delirium tremens characterized by tremors, confusion, agitation, hallucinations, and severe autonomic hyperactivity	Typically within 72-96 hours after the last drink. But can see delayed signs after about 5-10 days if untreated.

Step 3: Describe management of alcohol withdrawal

- Alcohol withdrawal treatment is multimodal and includes fluid and electrolyte repletion, medications, and vitamin supplementation including B-complex vitamins (thiamine, folate) and multivitamins.
- Alcohol use disorder is commonly associated with thiamine deficiency.
    - Thiamine deficiency can manifest as Wernicke's encephalopathy characterized by confusion, ophthalmoplegia/nystagmus, and ataxic gait (typically broad-based). However, many individuals with Wernicke's encephalopathy do not present with all three of the classic symptoms. Wernicke's encephalopathy can progress to Korsakoff syndrome, characterized as behavioral abnormalities and memory disturbances that affect both anterograde and retrograde memory. They are grouped collectively as Wernicke-Korsakoff syndrome.
    - During the initial states of managing alcohol withdrawal symptoms, it is imperative to supplement with thiamine prior to glucose administration to prevent Wernicke-Korsakoff syndrome. Thiamine supplementation can reverse many of the acute symptoms of Wernicke's encephalopathy; however, certain chronic neuropsychiatric sequelae of previous thiamine deficiency can persist despite appropriate treatment. Wernicke's encephalopathy should be treated with IV thiamine preferably but intramuscular (IM) or oral (PO) administration can be used if IV is unavailable. A consensus does not exist about dose of thiamine supplementation. The author recommends 500 mg three times daily for 3 consecutive days, then 250 mg once daily

for 5 consecutive days.

- Alcohol withdrawal can be measured by scales such as Clinical Institute Withdrawal Assessment for Alcohol Revised (CIWA-Ar).
    - The CIWA-Ar measures the severity of alcohol withdrawal. Cumulative scores of less than 8-10 indicate mild withdrawal, 8-15 indicate moderate withdrawal, and 15 or higher indicate severe withdrawal with impending possible delirium tremens.
- Alcohol withdrawal delirium is a diagnosis of exclusion; thus, it is essential to rule out other causes of delirium when assessing the patient.
- Treatment of alcohol withdrawal traditionally involves the use of medications that bind to the $GABA_A$ receptor to mitigate withdrawal symptoms and to reduce the risk of progression to seizures or delirium.
    - *Benzodiazepines*
        - Benzodiazepines remain the mainstay of treatment for alcohol withdrawal.
        - Respiratory status and mental status need to be monitored with benzodiazepine use.
        - Long-acting agents (chlordiazepoxide and diazepam) produce a smoother withdrawal due to the sustained effects of the drug and of its active metabolites produced by phase I liver oxidation.
        - Lorazepam represents the drug of choice in the elderly and those with liver disease, because lorazepam is not dependent on phase I metabolic reactions such as oxidation, which are compromised in the elderly and those with liver disease. Lorazepam also lacks active metabolites. Thus, risk of sedation, falls, and respiratory depression are minimized if lorazepam is used.
        - Benzodiazepine strategies include symptom triggered, fixed regimen, and front-loading strategies.
        - *Symptom-triggered approach*
            - Involves using medications only when the patient is symptomatic
            - Recommended for the majority of cases of alcohol withdrawal
            - Patients require less medication overall and usually require shorter treatment periods.
            - CIWA-Ar measures are used hourly for moderate withdrawal cases and Q 4-6 hours in stable withdrawal cases. When a score is above 8 on CIWA-Ar, medication is typically given depending on the score.
            - Typically, as needed (PRN) PO medications are given for scores between 8-15 and parenteral medications (IV/IM) are given for scores of 16 or above.
        - *Fixed-schedule approach*
            - If monitoring of withdrawal symptoms cannot be accurately performed due to inadequate staffing or training, if complicated withdrawal is anticipated based on history, or if co-morbid illnesses pose risk of a complicated hospital course with poor control of alcohol withdrawal, then fixed-schedule approaches are recommended.
            - Lorazepam 1-4 mg every 4-6 hours or Chlordiazepoxide 25-50 mg PO every 6-8 hours, or diazepam regimen 10-20 mg every 6-12 hours on the on hospital day one are recommended. These medications are then tapered over the hospital course.

        - *Front-loading approach*
            - Administration of a moderate-to-high dose of a long-acting benzodiazepine to produce sedation.
                - Drug levels auto-taper over time.
                - Risk of toxicity is high during early phase of treatment and close clinical monitoring is required.
                - Most appropriate for patients who are at increased risk to develop severe alcohol withdrawal complications (withdrawal seizures, DTs) based on history
    - *Phenobarbital*: Used is cases refractory to benzodiazepines. Phenobarbital has $GABA_A$ agonistic and anti-glutamatergic activity. It is dosed according to the patient's weight and overall withdrawal risk.
    - *Neuroleptics:* May be used as an adjunct to treat psychotic symptoms or agitation, but caution is advised as these agents can lower seizure threshold
    - *Dexmedetomidine*: May be used as an adjunct to dampen the noradrenergic surge in alcohol withdrawal. ICU monitoring is required.
    - *Propofol*: Used as an adjunct in cases of severe alcohol withdrawal that is refractory to standard treatments. Ventilation is often required, and propofol is typically administered in ICU.

Step 4: Assess motivation for change and engage patient in recovery services

- Hospitalization for alcohol withdrawal can be a turning point for patients and can present an opportunity for insight about alcohol use disorder and steps involved in recovery.
- Motivational interviewing can assess readiness for change.
    - If patients are ready, they can be linked and engaged in treatment for alcohol use disorder. A variety of treatment approaches are available such as medication-assisted treatment, psychotherapy, 12-step programs, and other forms of peer support. Treatment should be tailored based on patient needs, preferences, and resource availability.

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