

CASE: 67 yo homeless man with long history of alcohol dependence is brought to the ED for confusion and ataxia. Past medical history is notable for alcohol withdrawal seizures, Hepatitis C, and gout. Blood alcohol level (BAL) is 357 mg/dl. Other labs include: BUN 34, Cr 1.3, K⁺ 2.9, Mg⁺⁺ 1.4. How should you manage this patient initially?

Alcohol Withdrawal in the Hospitalized Patient

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Alcohol Withdrawal Syndromes:

- Tremulousness or minor withdrawal symptoms occur within 6-12 hours of decline in blood alcohol level (BAL) with symptoms peaking at 24-36 hours. This is due to central nervous system and sympathetic hyperactivity with resultant tremors, anxiety, insomnia, anorexia, gastrointestinal upset, diaphoresis, palpitations, headache
- Alcoholic hallucinosis occurs in approximately 25% of hospitalized patients who have a prolonged history of alcohol abuse. It typically occurs within 24 hours of abstinence and tends to consist of visual disturbances, but may be auditory or tactile in nature. Sensorium is otherwise intact. Occurs earlier than Delirium Tremens (DT's) and is not a predictor of DT's.
- Withdrawal seizures typically occur within 8-48 hours and are usually generalized tonic clonic seizures. This complication occurs in 5-33% of chronic alcoholics and is more common in those with history of withdrawal seizures or in untreated patients. Less than 3% evolve into status epilepticus.
- DT occurs in 5% of patients with alcohol withdrawal. It is a potentially life-threatening syndrome associated with autonomic hyperactivity, delirium, hyperthermia, hypertension, tachycardia, diaphoresis, and volume depletion. It typically begins 3-5 days after the last drink and lasts for 1-5 days. Risk factors for DT's include a history of sustained drinking, history of previous DT's, age > 30, and concurrent illness. Respiratory failure and cardiac arrhythmias are the most common causes of death. Mortality is increased with delayed diagnosis and treatment as well as comorbid conditions.
- Admission to ICU should be considered for any patient with hemodynamic instability, respiratory compromise, or frequent need for high dose sedatives or IV infusion of a sedative to control symptoms.

Wernicke's encephalopathy:

- Triad of confusion, ataxia, and ophthalmoplegia that occurs in malnourished alcoholics who receive glucose containing infusions prior to receiving thiamine. Thiamine deficiency is reported to occur in up to 30-80% of alcohol dependent patients. Thiamine is a necessary cofactor for glucose metabolism.

Korsakoff's syndrome:

- An amnesic disorder also caused by thiamine deficiency and is commonly associated with confabulation. Again, thiamine administration must precede or accompany glucose infusions.

Clinical severity scale:

- CIWA-Ar is the Clinical Institute Withdrawal Assessment for Alcohol scale. It is a well-validated 10-item scale. Scores of < 15 indicate mild withdrawal, 16-20 indicate moderate withdrawal, and > 20 indicates severe withdrawal. The 10 items monitored include nausea and vomiting, tremor, sweating, anxiety, agitation, tactile disturbances, auditory disturbances, visual disturbances, headache, and orientation/sensorium.

Treatment:

- Volume resuscitation and electrolyte correction (particularly potassium and magnesium).

- Thiamine 100 mg iv/im/oral daily for 3-5 days to prevent potential encephalopathy. Thiamine should be given prior to glucose-containing solutions since thiamine is a cofactor for several key enzymes in energy metabolism. Thiamine requirements are increased with high glucose intake. Encephalopathy may be precipitated in susceptible patients without prompt administration.
- Benzodiazepines are the drugs of choice to decrease symptoms, incidence of seizures, and DT's. These sedative hypnotics have proven safety and efficacy in well-designed randomized trials. Benzodiazepines act by increasing the affinity of the neurotransmitter GABA to their respective receptors.
 - ❑ No single benzodiazepine has been shown to be more effective than another.
 - ❑ Longer acting agents such as chlordiazepoxide and diazepam may provide a smoother withdrawal course with fewer breakthroughs, but they also increase the risk of excessive sedation in susceptible patients (i.e. elderly and in those with liver disease). Both of these agents have long half-lives and are metabolized by the liver to active metabolites.
 - ❑ Shorter acting agents such as lorazepam may be preferable in elderly patients and in those with liver disease because they are less likely to accumulate upon repeated administration. Lorazepam has an intermediate half-life and is metabolized in the liver to inactive metabolites.
 - ❑ Lorazepam is preferred over diazepam if the IM route is necessary due to better bioavailability and a quicker onset of action (diazepam is a poor IM drug due to lipophilicity).
 - ❑ Diazepam has a quicker onset and has better bioavailability than lorazepam when given orally.
- Dosing schedules for benzodiazepines include a fixed-schedule and a symptom-triggered schedule.
 - ❑ Fixed-schedule: Benzodiazepines given at fixed intervals over 72 hours even if symptoms are absent with additional doses given as needed for withdrawal symptoms. Examples: chlordiazepoxide 50mg oral q6h for 24 hours, then 25mg oral q6h for 48 hours, or lorazepam 2mg oral q6h for 24 hours followed by 1mg oral q6h for 48 hours.
 - ❑ Symptom-triggered: Benzodiazepines administered only when the patient is having withdrawal symptoms (i.e. CIWA score \geq 8-10). Initially lorazepam 1-4mg IV or diazepam 5-10mg IV can be given at 10-15 minute intervals until light sedation is achieved. Additional doses are then given at 1-2 hour intervals as necessary. Larger doses may be required for some patients.
 - ❑ Symptom-triggered approach is associated with a decrease in quantity of medication and the duration of treatment. Preferred strategy if lower risk of seizures or DTs.
 - ❑ Fixed-schedule approach is most useful in patients at high risk of major withdrawal symptoms, such as those with a history of prior withdrawal seizures or DTs.
- Other agents (second-line) include barbiturates, propofol, paraldehyde, carbamazepine, and baclofen.
 - ❑ Barbiturates may be an option in patients refractory to escalating doses of benzodiazepines. Phenobarbital is lacking well-designed trials demonstrating efficacy and safety. Phenobarbital has been shown to have an increased incidence of respiratory depression and coma during treatment than benzodiazepines. Phenobarbital has a very long half-life (~ 80-120 hours). Phenobarbital 130-260mg IV initially with a repeat dose of 130mg at 30-60 minutes if necessary to attain light sedation.
 - ❑ Propofol may also be effective in those refractory to increasing doses of benzodiazepines. Propofol modulates both GABA and NMDA receptors thus acting in a slightly different pathway than benzodiazepines. Propofol has a short half-life.
- Addiction services and alcohol abstinence counseling should be offered to all patients.

Clinical Pearls:

- Suspect alcohol withdrawal in every unexplained case of delirium and elevated blood pressure in the hospital.
- Withdrawal syndromes can co-exist or be mimicked by other conditions.
- Give thiamine prior to any infusion containing glucose.
- Do not delay diagnosis; treatment is more difficult if delayed.
- Lorazepam may be preferred in elderly patients and in those with liver impairment.
- Be cautious about treating hypertension as blood pressure will likely decrease once withdrawal is controlled.

Case Follow-up: The patient was placed on CIWA protocol with scheduled lorazepam. Lorazepam was given Q six hours for a 3-day taper along with prn lorazepam for breakthrough withdrawal symptoms. Potassium (40 meq) and magnesium (2 grams) were added to IV fluids. Thiamine 100mg and a multivitamin with folate were administered daily. The patient had episodes of hypertension and tachycardia that responded to lorazepam indicating these were signs of withdrawal. The patient became more oriented on hospital day 2 and progressed well until discharge on hospital day 4 without complications. He received counseling regarding abstinence.

References:

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