

Phenobarbital for management of alcohol withdrawal

Chronic alcohol use causes down-regulation of GABA receptors and up-regulation of NMDA receptors, the site of action for glutamate. When alcohol consumption is stopped or decreased, the combination of enhanced stimulation and impaired inhibition results in the psychomotor agitation and autonomic hyperactivity characteristic of alcohol withdrawal. The standard of care for alcohol withdrawal treatment is symptom-triggered benzodiazepines until clinical improvement is achieved. However, this strategy may not be effective in patients with severe alcohol withdrawal and some patients develop symptoms that are refractory to high doses of benzodiazepine therapy. Phenobarbital, a barbiturate, has been studied in the management of alcohol withdrawal and has been used as an alternative or adjunctive treatment with benzodiazepines. Benzodiazepines work by enhancing the effects of GABA by increasing the frequency of channel opening at the GABA receptor. Phenobarbital works by prolonged channel opening at the GABA receptor and inhibiting NMDA receptors to decrease the symptoms of alcohol withdrawal.

Patient selection:

1. Patients at risk for severe alcohol withdrawal based on the Prediction of Alcohol Withdrawal Severity Scale (PAWSS) are potential candidates for the phenobarbital protocol. The PAWSS was validated in medically ill inpatients and a score greater than or equal to 4 has good sensitivity and specificity for predicting patients who are at risk for developing severe alcohol withdrawal symptom (CIWA score greater than 15). The PAWSS score must be completed/documentated prior to initiating the phenobarbital protocol.
2. Risk factors for phenobarbital complications
 - a. Risk of sedation
 - i. Greater than 65 years of age
 - ii. Hepatic dysfunction or cirrhosis
 - iii. Concomitant recent benzodiazepines, opioids, or other sedatives
 - iv. Head injury
 - b. Risk of respiratory compromise
 - i. Pneumonia
 - ii. Coexisting pulmonary disease:
 1. COPD
 2. Asthma
 3. Interstitial lung disease
 4. Pulmonary fibrosis
 - iii. Rib fractures
 - iv. Chest tube(s)
 - v. Pulmonary contusion(s)
 - vi. C-collar / brace
 - c. Risk for drug accumulation / toxicity
 - i. Severe liver disease / cirrhosis
 - ii. Acute or chronic renal disease
 - iii. Combined liver and renal disease
3. Concomitant sedative medications increase the risk of respiratory depression with phenobarbital
 - a. Scheduled or symptom-triggered benzodiazepines may not be administered concomitantly with the phenobarbital protocol for alcohol withdrawal unless the patient is in the ED or ICU
 - b. Minimize the use of all sedating medications
 - c. In general, if patient takes home opioids, it is appropriate to continue stable home dose to prevent withdrawal symptoms

4. Signs of barbiturate toxicity
 - a. Hypotension
 - b. Bradycardia
 - c. CNS depression
 - d. Respiratory depression

Documentation:

1. PAWSS score must be completed and documented prior to initiating phenobarbital
2. Administration of phenobarbital doses must be documented on the MAR
3. Vitals signs and CIWA scores must be documented as ordered

References:

1. Maldonado JR, Sher Y, Das S, Hills-Evans K, Frenklach A, et al. Prospective validation study of the prediction of alcohol withdrawal severity scale (PAWSS) in medically ill inpatients: a new scale for the prediction of complicated alcohol withdrawal syndrome. *Alcohol and Alcoholism* 2015; 50(5): 509-18.
2. Wood E, Albarqouni L, Tkachuk S, Green C, Ahamad K, et al. Will this hospitalized patient develop severe alcohol withdrawal syndrome? The rational clinical examination systemic review. *JAMA*. 2018;320(8):825-33.
3. Hammond DA, Rowe JM, Wong A, Wiley TL, Lee KC, et al. Patient outcomes associated with phenobarbital use with or without benzodiazepines for alcohol withdrawal syndrome: a systemic review. *Hospital Pharmacy* 2017; 52(9): 607-16.
4. Yoonsun M, Thomas MC, Karras GE. Barbiturates for the treatment of alcohol withdrawal syndrome: a systemic review of clinical trials. *Journal of Critical Care* 2016; 32: 101-7.
5. The Ohio State University alcohol withdrawal clinical practice guidelines 2016.
6. Portsmouth Regional Hospital phenobarbital for moderate to severe alcohol withdrawal in the acute care setting. HealthTrust educational Webinar 2017.