Maine Medical Center Trauma Clinical Practice Guideline (MMCT-CPG)

Phenobarbital in the management of the non-ICU Trauma patient at risk of/ or experiencing severe alcohol withdrawal

(MMC-CPG ID: 2023-09)

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First Publication Date	Revision Date	Supersedes CPG dated
6/1/2012	November 2023	11/6/2018

Guidelines translate best evidence into best practice. A well-crafted guideline promotes quality by reducing healthcare variations, improving diagnostic accuracy, promoting effective therapy, and discouraging ineffective – or potentially harmful – interventions.

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PURPOSE

The purpose of this guideline is to identify and treat those patients who are at high risk of severe alcohol withdrawal, or who are already demonstrating severe alcohol withdrawal. Treatment guidelines for this population are provided. In order to begin this treatment pathway, definite diagnosis of alcohol withdrawal must be confirmed and all benzodiazepine orders for the treatment of alcohol withdrawal must be discontinued.

For patients felt to be at risk for alcohol dependence or withdrawal, it is recommended that consideration be given to a Substance Abuse consultation and/or providing the patient with contact information for outside resources for help.

BACKGROUND

Diagnosis of Alcohol Withdrawal - Inclusion Criteria*:

1. Patient is an active drinker (within the last 30 days) with a history of previous alcohol withdrawal or has a positive BAL on admission AND has a history of alcohol withdrawal seizures and/or delirium tremens. OR
2. CIWA score >16 AND a history of alcohol use AND symptom onset within 48 hours of last drink

*Additional high risk inclusion criteria may be considered per provider discretion.

PRACTICE MANAGEMENT GUIDELINE

Treatment:

1.) Phenobarbital

Loading (Day 1):

- Low risk* of sedation and respiratory compromise:

Phenobarbital 7.5 mg/kg (based on actual body weight) IV infused over 1 hour ONCE

- High risk*: of sedation and respiratory compromise:

Phenobarbital 2.5 mg/kg (based on actual body weight) IV q2h x 3 doses for a total dose of 7.5 mg/kg

*Risk of sedation or respiratory compromise:

- >65 years of age
- Documented obstructive sleep apnea or risk factors (significant facial and cervical obesity, high Mallampati score of III or IV)
- Hepatic dysfunction (AST or ALT > 3 times the upper limit of normal) or cirrhosis

- Concomitant (within 12 hours) opioids, benzodiazepines, or other sedatives that may suppress respiratory drive
- Pneumonia
- Chronic obstructive pulmonary disease (COPD)
- Asthma
- Interstitial lung disease or pulmonary fibrosis
- Pneumonia
- Chronic obstructive pulmonary disease (COPD)
- Asthma
- Interstitial lung disease or pulmonary fibrosis
- Head/ neck cancer
- Rib fractures and/or pulmonary contusion(s)
- C-collar/brace
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Maintenance doses (Day 1-4):

Maintenance Dose [a]	**Weight <80 kg**	**Weight ≥80 kg**
Day 1-2 (begin 3 hr after final loading dose)	PHENobarbital 97.2 mg PO q8h x 3-6 doses, or PHENobarbital 90 mg IV q8h x 3-6 doses	PHENobarbital 129.6 mg PO q8h x 3-6 doses, or PHENobarbital 130 mg IV q8h x 3-6 doses
Day 3	PHENobarbital 97.2 mg PO q12h x 2 doses, or PHENobarbital 90 mg IV q12h x 2 doses	PHENobarbital 129.6 mg PO q12h x 2 doses, or PHENobarbital 130 mg IV q12h x 2 doses
Day 4	PHENobarbital 97.2 mg PO q24h x 1 dose, or PHENobarbital 90 mg IV q24h x 1 dose	PHENobarbital 129.6 mg PO q24h x 1 dose, or PHENobarbital 130 mg IV q24h x 1 dose
Breakthrough Dosing[b] **(Days 1-4)**	PHENobarbital 90 mg IV q2h prn agitation, anxiety, restlessness. Notify provider if more than 2 doses are needed in a 6 hr period.	PHENobarbital 130 mg IV q2h prn agitation, anxiety, restlessness. Notify provider if more than 2 doses are needed in a 6 hr period.

[a] If a scheduled dose of PHENobarbital is held due to over-sedation, increase the interval it is being administered (e.g. increase from q8h to q12h, q12h to q24h).

[b] Do not use CIWA to determine need for breakthrough medication. If 2 or more prn doses of PHENobarbital are required, continue maintenance PHENobarbital dose at q8h for an additional day.

Additional considerations:

- The oral bioavailability of PHENobarbital is >95%. Intravenous route of administration for maintenance dosing should be reserved for patients who are unable to swallow or do not have enteral access.
- The onset of action of IV PHENobarbital is 5 minutes with peak effect >15 minutes. The onset of action of oral PHENobarbital is >60 minutes. There are no contraindications to administering IV PHENobarbital on the floor or in intermediate care areas.

- Therapeutic drug monitoring of PHENobarbital is not routinely indicated. A serum level may be warranted in the following circumstances: total daily dose exceeds 10 mg/kg, severe liver disease or cirrhosis, acute renal failure or end- stage renal disease, symptoms of barbiturate toxicity (hypotension, bradycardia, severe CNS or respiratory depression). If serum concentration exceeds 40 mcg/mL, dose should be reduced.
- PHENobarbital is relatively well tolerated with a low incidence of side effects. Respiratory depression requiring intubation is infrequent (< 5%) at the doses utilized for alcohol withdrawal. CNS depression may occur if given in conjunction with other centrally-acting medications. Other rare side effects include Stevens-Johnson syndrome, DRESS and transaminitis.
- PHENobarbital is an inducer of CYP3A and CYP2C enzymes, therefore drug interactions must be considered. It is important to note the induction may be delayed in onset and offset of more than a week.

2.) Clonidine

- If the patient is experiencing autonomic symptoms due to alcohol withdrawal (e.g. tachycardia, hypertension, tremors, sweating, nausea/vomiting), schedule clonidine.
- Hold parameters for clonidine: HR < 60 bpm, SBP < 100 mmHg
- Days 1 and 2: Clonidine 0.2 mg PO/SL q6h x 8 doses
- Day 3: Clonidine 0.2 mg PO/SL q8h x 3 doses
- Day 4: Clonidine 0.2 mg PO/SL q12h x 2 dose
- Day 5: Clonidine 0.2 mg PO/SL q24h x 1 dose
- If 2 or more prn doses of PHENobarbital are required, continue maintenance clonidine dose at q6h for an additional day

3.) Antipsychotics

•If the patient is experiencing hallucinations or disorientation, consider the addition of antipsychotics:

  - QTc < 500 ms: Haloperidol 2.5 mg IV q4h prn agitation (maximum dose in 24 hr: 30 mg)
  - QTc > 500 ms: Olanzapine 5 mg IM q6h prn agitation (maximum dose in 24 hr: 30 mg)

4. Vitamin Supplementation

- Thiamine 200 mg IV every 8 hours for 3-5 days followed by 100 mg PO daily for the prevention and/or treatment of Wernicke's encephalopathy
- Folic acid 1 mg IV/PO daily
- Multivitamin 1 tablet PO daily (optional - no evidence for routine supplementation)
- Monitor serum magnesium levels and replete as necessary
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5. Monitoring

- Obtain baseline liver function tests before initiating PHENobarbital.

- Monitor vitals every 4 hours
- Continue to document CIWA scores for clinical assessment of alcohol withdrawal course, but do not use it to determine the need for breakthrough medication)
- Obtain daily EKG if either antipsychotic is required,
- If agitation continues despite 2 prn doses of PHENobarbital, 15 mg of olanzapine or 10 mg of haloperidol, consider calling psychiatry for further recommendations. If patient is requiring frequent intervention, consider contacting the SCU coordinator for additional resources and consideration for transfer to higher level of care.
- If the patient is over-sedated, hold PHENobarbital dose and contact provider.

Summary of Treatment Guideline:

	Weight <80 kg	Weight ≥80 kg
Day 1-2	*Maintenance:* PHENobarbital 7.5 mg/kg IV load, given as a 1-hr infusion or divided q2h x 3 doses (depending on risk of sedation/respiratory compromise), followed by PHENobarbital 97.2 mg PO q8h x 3-6 doses, or PHENobarbital 90 mg IV q8h x 3-6 doses Clonidine 0.2 mg PO/SL q6h x 8 doses	*Maintenance:* PHENobarbital 7.5 mg/kg IV load, given as a 1-hr infusion or divided q2h x 3 doses (depending on risk of sedation/respiratory compromise), followed by PHENobarbital 129.6 mg PO q8h x 3-6 doses, or PHENobarbital 130 mg IV q8h x 3-6 doses Clonidine 0.2 mg PO/SL q6h x 8 doses
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Day 3	*Maintenance:* PHENobarbital 97.2 mg PO q12h x 2 doses, or PHENobarbital 90 mg IV q12h x 2 doses Clonidine 0.2 mg PO/SL q8h x 3 doses	*Maintenance:* PHENobarbital 129.6 mg PO q12h x 2 doses, or PHENobarbital 130 mg IV q12h x 2 doses Clonidine 0.2 mg PO/SL q8h x 3 doses
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Day 4	*Maintenance:* PHENobarbital 97.2 mg PO q24h x 1 dose, or PHENobarbital 90 mg IV q24h x 1 dose Clonidine 0.2 mg PO/SL q12h x 2 doses	*Maintenance:* PHENobarbital 129.6 mg PO q24h x 1 dose, or PHENobarbital 130 mg IV q24h x 1 dose Clonidine 0.2 mg PO/SL q12h x 2 doses
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Day 5	*Maintenance:* Clonidine 0.2 mg PO/SL q24h x 1 dose Discontinue PHENobarbital and antipsychotic prn orders, if appropriate	*Maintenance:* Clonidine 0.2 mg PO/SL q24h x 1 dose Discontinue PHENobarbital and antipsychotic prn orders, if appropriate

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