EVMS EM JC CRITICAL REVIEW FORM: THERAPY ARTICLES

Resident: Kyle Parker **Date:** 11/29/21

Citation: Tidwell WP, Thomas TL, Pouliot JD, Canonico AE, Webber AJ. Treatment of Alcohol Withdrawal Syndrome: Phenobarbital vs CIWA-Ar Protocol. Am J Crit Care. 2018 Nov;27(6):454-460. doi: 10.4037/ajcc2018745. PMID: 30385536.

Study Objective: To compare a benzodiazepine based CIWA-Ar protocol with a phenobarbital protocol for alcohol withdrawal.

Study Methodology: Retrospective cohort study that looked at EMR data before and after the institution of a phenobarbital protocol for alcohol withdrawal. Patients who had received either therapy protocol during the study period were identified by a report run in the electronic medical records system. An initial record search was conducted to identify patients who received the phenobarbital protocol, which began in 2017. At the time of collection, data through June 2017. The primary efficacy outcome was the difference in ICU length of stay (LOS) between the 2 protocols. Secondary outcomes measured included hospital LOS, use of invasive mechanical ventilation, and use of adjunctive and sedating agents to control AWS symptoms.

GUIDE	COMMENTS
I. Are the results valid?	
A. Did experimental and control groups begin the study with a similar prognosis?	Difficult to say, how symptomatic the patient's in each group were was not well elucidated.
1. Were patients randomized?	No
2. Was randomization concealed (blinded)? In other words, was it possible to subvert the randomization process to ensure that a patient would be "randomized" to a particular group?	No
3. Were patients analyzed in the groups to which they were randomized?	N/A
4. Were patients in the treatment and control groups similar with respect to known prognostic factors?	Yes. Demographic data that was reported showed no statistically sig. differences other than age. Patients in the phenobarbital group were on average 7 years younger. No differences in race, sex, comorbidities, hx. of DT's or withdrawal seizures were noted. No reporting on homelessness or insurance status.

5. Were patients aware of group allocation?	Unclear, likely no
6. Were clinicians aware of group allocation?	Yes
7. Were outcome assessors aware of group allocation?	Yes. The authors make no mention of blinding data assessors to study objective or the use of a standardized data collection form both of which can help reduce bias in retrospective studies.
8. Was follow-up complete?	No. The authors provide no follow-up data such as re-admission rates, mortality, post-discharge sobriety
What are the results ?	
1. How large was the treatment effect?	Primary endpoint of ICU length of stay was reduced in the phenobarbital group by 2 days. From 4.4 days in the CIWA-Ar group to 2.4 in the phenobarbital group (p=<.001). Other secondary outcomes include fewer hospital days 6.9 vs 4.3 (p=.004), fewer patients requiring mechanical ventilation (14 vs. 1 p=<.001), fewer patients requiring dexmedetomidine (17 vs. 4 p=.002).
2. How precise was the estimate of the treatment effect? (CI's?)	Not reported. The CIWA-Ar group has a larger SD of ICU days.

III **How can I apply the results to patient care?**	
1. Were the study patients similar to my patient?	No, African American patients were underrepresented (3%).Women were under-represented (27%) though this likely reflects national trends.
2. Were all clinically important outcomes considered?	For the most part, could have reported on seizures, hemodynamic instability, possibly days of sobriety post-discharge. Adverse events not well described and N was likely underpowered to report.
3. Are the likely treatment benefits worth the potential harm and costs?	Likely. There was a significant decrease in ICU and hospital length of stay. Fewer number of patients requiring ventilatory support. Also, a less nursing intensive protocol.

Limitations:
Retrospective study. Single hospital and ICU setting.
Not clear how clinicians decided to use phenobarbital vs CIWA-Ar protocol

Subjective diagnosis of alcohol withdrawal, inherent limitations of the CIWA scoring system which historically has poor inter-rater reliability (*kappa score*)
Primarily looks at patient's needing ICU care where there is a large portion of patients with alcohol withdrawal who aren't this sick.
Phenobarbital group also received benzos at "clinician discretion"
Benzo group not consistent with the choice of drug, they equated all to a standard lorazepam dose.
Only looked at oral phenobarbital. Did not qualify patients who were in phenobarbital group who needed adjunctive benzos.

Clinical Bottom Line:
Phenobarbital is a viable alternative for alcohol withdrawal compared to standard CIWA benzo protocols. This study used a phenobarbital protocol identical to the one in the Sentara order set. The fears of oversedation and respiratory depression with phenobarbital have not been demonstrated, in fact the opposite has been shown more often. Mechanism of action treats more of the symptoms of alcohol withdrawal than benzos which only work on GABA.