Maine Medical Center
Department of Emergency Medicine
Journal Club Summary Template

Date: 4/14/2022	**Presenter Name: Cynthia Gaudet PGY 2**

Article Citation: Rosenson J, Clements C, Simon B, et al. Phenobarbital for acute alcohol withdrawal: a prospective randomized double-blind placebo-controlled study. *J Emerg Med*. 2013;44(3):592-598.e2. doi:10.1016/j.jemermed.2012.07.056
Country(ies): United States
Funding Source(s):

Purpose
Research Question(s): Does a single dose of IV phenobarbital decreased ICU admissions in AAWS?
Hypotheses: A single dose of IV phenobarbital combined with a standardized, symptom-guided lorazepam-based alcohol withdrawal protocol would result in decreased intensive care unit admission.
Study Purpose: ***Secondary outcomes:***

Methods
Study Design: Prospective, randomized, double-blind, placebo-controlled study of ED patients with acute alcohol withdrawal syndrome (AAWS)
Outcome(s) ***[or Dependent Variable]:*** ***Primary outcome:*** - Initial and subsequent level of hospital care (ICU [1:2 nurse: patient] vs telemetry [1:3] vs floor [1:4]) **Secondary outcomes:** - Time of arrival in ED - Initial vital signs - Initial alcohol withdrawal clinical assessment (AWCA) score - Timing of initial lorazepam and study medication administration - Time until admission - Max AWCA score - Time of discharge - Prior AAWS hospital admissions - Incidence of seizures, intubation, falls, use of mechanical restraints, need for bedside sitter, and mortality
Intervention ***[or Independent Variable]:*** Phenobarbital administration
Ethics Review: IRB Review : Clinical Trials gov NCT 01884417 IACUC Review Other:
Research Setting: Urban ED w/ annual census of 85,000 patients EM residency program with PGY 1-4 (40 total residents) 17 attendings and 12 ED mid-level practitioners Jan 2009- March 2010
Study Subjects: All patients with suspected AAWS
Inclusion Criteria: - Age > 18 - Suspected AAWS (tachycardia [HR>100], tremor, paroxysmal sweats, agitation, anxiety, hallucinations, or clouded sensorium) - Provider judgment of clinical need for placement on the institutional lorazepam-based alcohol withdrawal protocol - Provider judgment of anticipated need for hospital admission for inpatient management of AAWS

Exclusion Criteria:
- Age <18
- Pregnancy
- Allergy to phenobarbital, lorazepam, phenytoin or carbamazepine
- Known severe hepatic impairment
- Inability to obtain IV access
- Primary admission diagnosis other than acute alcohol withdrawal

Study Interventions:
- all participants were placed on institutional symptom-guided lorazepam-based alcohol withdrawal protocol (which is a modified version of CIWA)
- Randomized to receive single dose of IV phenobarbital (10mg/kg in 100ml NS) or IV normal saline (both delivered same-sized, identical appearing covered plastic bags, prepped by pharmacy and administered over 30 min

Study Groups:
- phenobarbital
- Placebo (normal saline)

Instruments/Measures Used:
- **level of care at admission**
- **Time : length of stay (hospital admission to discharge)**
- **Use of continuous lorazepam**
- **Total amount of lorazepam per patient**
- **Incidence of adverse events**

Data Collection:

Data Analysis:

***A priori* sample size calculation?** Yes **No** Not Described N/A

Statistical analyses used:

Adjustment for potential confounders? Yes No Not Described N/A
If yes, list:

Results
Study participants:

Brief answers to research questions *[key findings]:*

- *single dose of IV phenobarbital had decreased ICU admission rate (8% vs 25% in placebo group); [95% CI 4-32%]*
- No difference in telemetry or floor admissions
- No difference in median ICU or total hospital LOS

- Phenobarb resulted in decreased use of continuous lorazepam infusion (4% vs 31% in placebo group; [95% CI 14-41%])
- Phenobarb decreased total lorazepam required (26 mg vs 49mg in placebo); [95% CI 7-40]

Additional findings:

- No study participant transferred to higher level of inpatient care
- No difference in incidence of adverse outcomes: intubation, seizure, mechanical restraints, or bedside sitter
- No falls or mortality in either group
- No difference in adjunct medications between the two groups: morphine, fentanyl, hydromorphone, propofol, and haloperidol

Limitations:

- Single county ED
- 1 year of enrollment
- Low percentage of available patients actually enrolled
- Enrollment relied on ED provider judgment: decision to admit to ICU, start continuous lorazepam infusion. No standardized protocol, provider dependent decisions (although these providers were all blind to treatment group). Did no formally asses inter-rater reliability regarding ICU admission
- Modified CIWA — AWCA scale which is **unvalidated**
- Phenobarbital 10 mg/kg dose was largest dose approved by IRB and may not be optimal regimen
- Patient weight estimated
- 89% of student participants were male

Other thoughts:

- No a priori sample size calculation - ?uncertain if sufficiently powered
- Clinical significance - did not appear to have difference in adverse outcomes but also did not mention or quantify autonomic derangement, delirium or seizures; hypotension, respiratory depression
- **Limited patient characteristics: time since last drink, presentation ethanol level, liver function tests, and other co-morbid conditions**
- **Half the study subjects eligible but did not get analyzed from both groups (did not consent, alcohol withdrawal not primary admission diagnosis, not admitted)**

Clinical Implications
Applicable? **Not yet - limitation in study are important to consider before changing practice** **Repeat studies, validation of their modified CIWA, expanding data collection** **Feasible?** **Yes** **Clinically relevant?** *Yes - AAWS is a daily faced CC* *Adjunct therapy for anticipated severe alcohol withdrawal* **Comments:**

Level of evidence generated from this study
Ia: evidence obtained from meta-analysis of randomized controlled trials Ib: evidence obtained from at least one randomized controlled trial IIa: evidence obtained from at least one well-designed, controlled study without randomization IIb: evidence obtained from at least one other type of well-designed quasi-experimental study III: evidence obtained from a well-designed, non-experimental study IV: expert committee reports; expert opinion; case study; case report

Additional Comments/Discussion/Notes