A Pre/Post Implementation Study: Assessing the Addition of Phenobarbital to the Alcohol Withdrawal Protocol

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Disclosure Statement

These individuals have the following to disclose concerning possible financial or personal relationships with commercial entities (or their competitors) that may be referenced in this presentation

- Caitlin Casper, PharmD: nothing to disclose
- Cristy Gaddy, PharmD, BCPS: nothing to disclose
- Sophia Braun, PharmD, BCPS: nothing to disclose
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Northeast Georgia Medical Center

- 850+ Bed Community Health System
  - 5 Hospital Locations
  - Serving 1.4 Million+ Patients
- Graduate Medicine Education System
  - 200+ Resident Physicians
  - 6 specialties
- Level I Trauma Center
- Comprehensive Stroke Center

BACKGROUND

- 75 million people worldwide have an alcohol use disorder
  - Harmful use of alcohol accounts for 3 million deaths annually
  - Rate of all alcohol-related emergency department visits increased 47.0% between 2006 and 2014 in the United States.
- The brain compensates for chronic alcohol use through:
  - Downregulation of Gamma-aminobutyric acid (GABA), an inhibitory receptor, which leads to decreased neuronal activity
  - Upregulation of N-Methyl-D-aspartate (NMDA), an excitatory receptor, which lead to increased neuronal activity
- Abrupt decreases in consumption of alcohol increases excitatory neural activity leading to alcohol withdrawal syndrome (AWS)

(WHO. *Harmful use of Alcohol.* 2018.)
(Jesse,S. et al. Acta Neurol Scand. 2017.)
(NIAAA."Alcohol-Related Emergencies and Deaths in the United States". 2024.)

BACKGROUND

- Benzodiazepines (BZDs) are the mainstay treatment for alcohol withdrawal syndrome
- Phenobarbital (PH) has a longer half-life and a dual mechanism of action:
  - Enhances the inhibitory effects of GABA
  - Inhibits the excitatory effects of glutamate

Alcohol Benzo Withdrawal CIWA [304100215]

CIWA Score	Vital Signs and CIWA	Chlordiazepoxide (Librium) Oral	Clorazepate (Tranxene) Oral	Phenobarbital Oral	Lorazepam (Ativan) Oral Patients greater than or equal to 65 years; History of cirrhosis or total bilirubin greater than 2	Lorazepam (Ativan) IV Patient greater than or equal to 65 years; History of cirrhosis or total bilirubin greater than 2	Phenobarbital IV (up to 20 mg/kg cumulative)
Prevention		25 mg once	7.5 mg once	200 mg once OR Phenobarbital IV 195 mg once for PAWSS 1-3			PAWSS 4 or more: 10 mg/kg loading dose
0 to 5	Q 4 HR	No Treatment	No Treatment	No Treatment	No Treatment	No Treatment	No Treatment
6 to 8	Q 4 HR	25 mg Q 1 H PRN	7.5 mg Q 4 H PRN	100 mg Q 1 H PRN	1 mg Q 2 H PRN	1 mg Q 30 MIN PRN	130 mg Q 30 MIN PRN
9 to 15	Q 2 HR	100 mg Q 1 H PRN	7.5 mg Q 2 H PRN	200 mg Q 1 H PRN	2 mg Q 2 H PRN	2 mg Q 30 MIN PRN	130 mg Q 30 MIN PRN
16 to 25	Q 1 HR					4 mg Q 30 MIN PRN	260 mg Q 30 MIN PRN
26 or greater	Q 30 MIN					4 mg Q 30 MIN PRN	260 mg Q 30 MIN PRN

Vital sign reassessment 2 hours after oral PRN dose given OR 1 hour after IV PRN dose given

(Wong et al., *Journal of Addiction Med*. 2020.)
(Tidwell, W. P. et al.,*American Journal of Critical Care.* 2017)
(Alwakeel, M. et al., *Critical Care Explorations.* 2023)

PURPOSE

The purpose of this quality improvement project was to assess the clinical effect of adding phenobarbital to our Clinical Institute Withdrawal Assessment for Alcohol (CIWA) protocol

STUDY DESIGN

- IRB approved December 2023

- A pre-post implementation retrospective chart review
  - Pre-Implementation: Jan 1st 2022 to Nov 30th 2022
  - Post-Implementation: Jan 1st 2023 to Nov 30th 2023

- Patients were identified using reports generated from the electronic health record

STUDY DESIGN

- INCLUSION CRITERIA
  - ≥ 18 years of age
  - Admission with a primary diagnosis of alcohol withdrawal
- EXCLUSION CRITERIA
  - No alcohol withdrawal CIWA protocol ordered at admission
  - Pregnant and vulnerable populations
- STATISTICAL ANALYSIS
  - Categorical variables
    - n, %
    - Chi-square or Fisher's exact test
  - Continuous or ordinal variables
    - Medians and interquartile ranges (IQR)
    - Mann-Whitney U test

METHODS

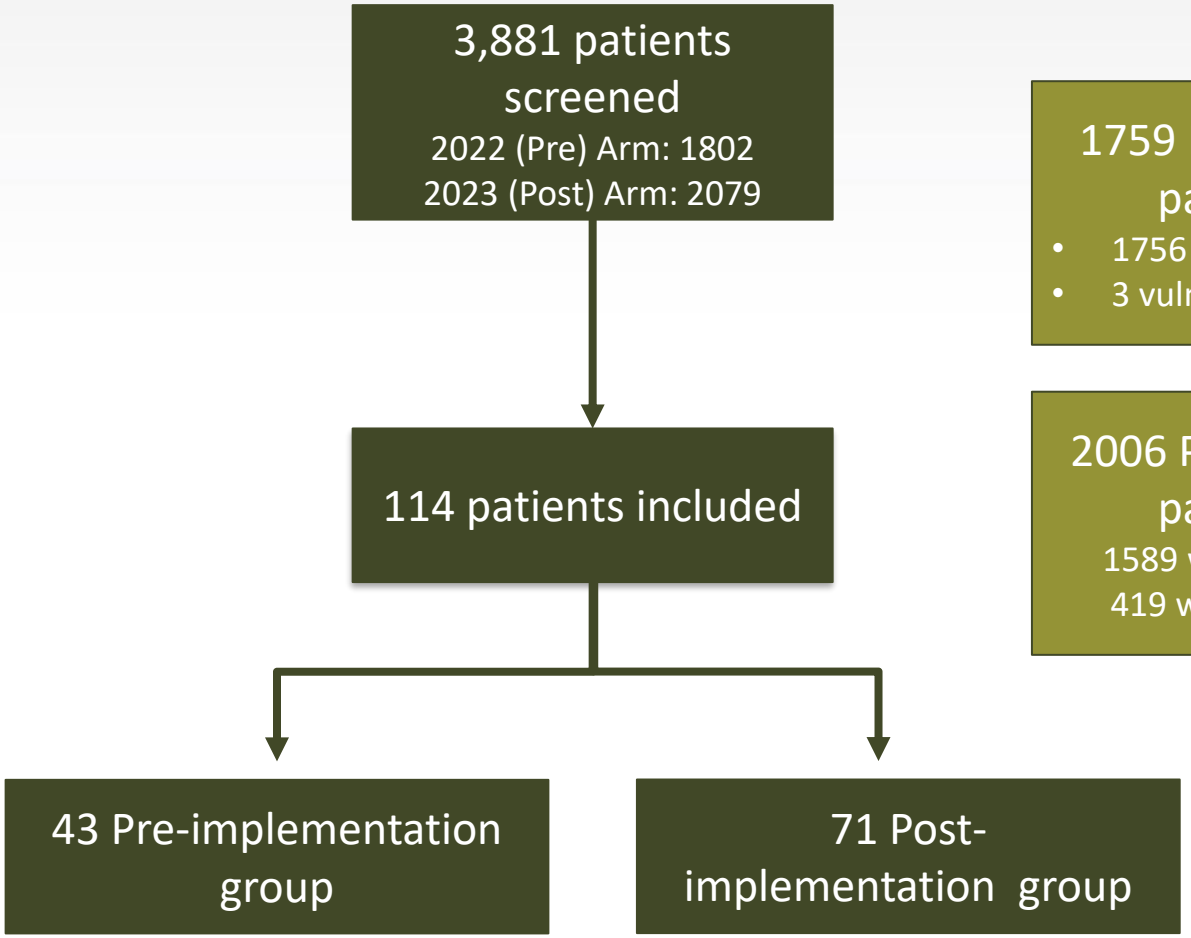
PRIMARY ENDPOINT

- Hospital length of stay (LOS)

SECONDARY ENDPOINTS

- Need for ICU admission
- Adjunctive agents (AA) used
- Need for mechanical ventilation
- Change in CIWA score at > 24 hours admission

STUDY POPULATION



1759 Pre-implementation patients excluded

- 1756 w/out primary diagnosis
- 3 vulnerable population patients

2006 Post-implementation patients excluded

1589 w/out primary diagnosis
419 w/out PH administration

BASELINE CHARACTERISTICS

Characteristic	Pre-Implementation (2022) n=43	Post-Implementation (2023) n=71	p-value
Age, years (IQR)	51 (42, 60)	47 (38, 59)	0.20
Male, n (%)	33 (76.7)	53 (74.6)	0.80
Weight, kg (IQR)	82 (69.5, 92)	81.8 (69.8, 92.4)	0.80
Race, n (%)			
White	34 (79.1)	61 (85.9)	0.34
Black	4 (9.3)	4 (5.6)	0.47
Asian	1 (2.3)	—	0.38
Other	4 (9.3)	6 (8.5)	>0.99
Comorbidities, n (%)			
Diabetes	5 (11.6)	9 (12.7)	0.87
Hypertension	29 (67.4)	45 (63.4)	0.66
Hyperlipidemia	9 (20.9)	24 (33.8)	0.14
COPD	4 (9.3)	4 (5.6)	0.47
Liver Disease	9 (20.9)	16 (22.5)	>0.99
Seizure Disorders	8 (18.6)	16 (22.5)	0.62
Psychiatric Disorders*	28 (65.1)	33 (46.5)	0.05
Charlson Comorbidity Index			
CCI=0	16 (37.2)	31 (43.7)	0.50
CCI ≤ 2	14 (32.6)	22 (31.0)	0.86
CCI ≥ 3	13 (30.2)	18 (25.4)	0.57

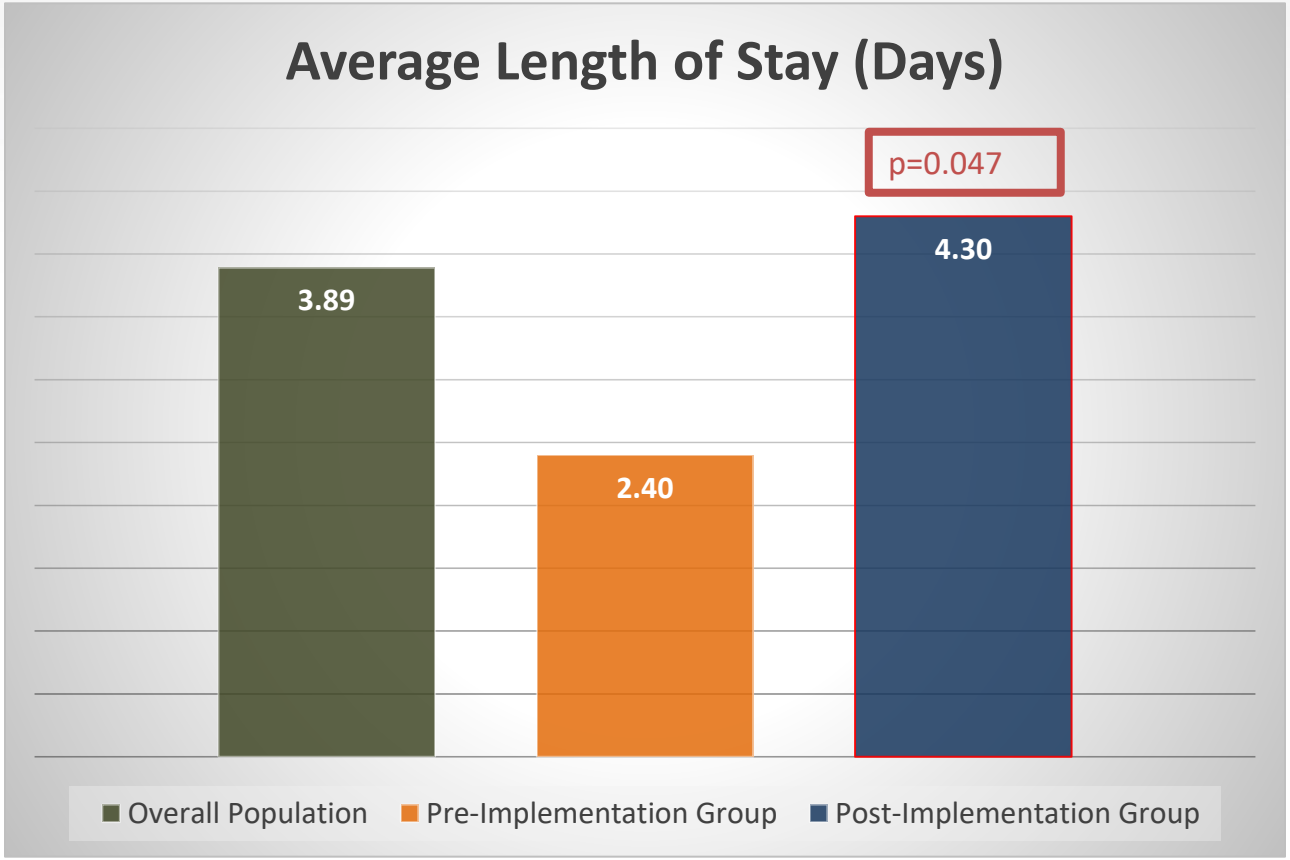
Values listed as median (IQR) or value (percentage)
*indicates statistically significant difference

AWS CHARACTERISTICS

Characteristic	Pre-Implementation (2022) n=43	Post-Implementation (2023) n=71	p-value
Initial CIWA Score, n (%)			
Mild (0-9)	19 (44.2)	26 (36.6)	0.42
Moderate (10-15)	11 (25.6)	19 (26.8)	0.89
Severe (≥ 15)	12 (27.9)	23 (32.4)	0.62
Unknown/Not recorded	1 (2.3)	3 (4.2)	>0.99
Admission Location, n (%)			
ICU	3 (7)	6 (8.5)	>0.99
Floor*	23 (53.5)	51 (71.8)	0.05
Emergency Department only*	17 (39.5)	14 (19.7)	0.02

Values listed as median (IQR) or value (percentage)
*indicates statistically significant difference

PRIMARY ENDPOINT



SECONDARY ENDPOINTS

Secondary Outcomes	Pre-Implementation (2022) n=43	Post-Implementation (2023) n=71	p-value
Need for Mechanical Ventilation, n (%)	1 (2.3)	3 (4.2)	>0.99
Need for ICU Admission, n (%)	1 (2.3)	4 (5.6)	0.65
Need for Adjunctive Agents, n (%) *	2 (4.7)	14 (19.7)	0.03
Adjunctive Agents Used, n (%)			
Valproate	—	1 (1.4)	>0.99
Dexmedetomidine *	2 (4.7)	13 (18.3)	0.04
Midazolam	—	3 (4.2)	0.29
Propofol	1 (2.3)	1 (1.4)	>0.99
Ketamine	—	1 (1.4)	>0.99
Average BZD dose in lorazepam equivalents, mg	15.2	25.3	0.78
Need for BZD dosing, n (%) *	42 (97.7)	56 (78.9)	0.005

Values listed as median (IQR) or value (percentage)
*indicates statistically significant difference

CIWA SCORE ≥ 24 HOURS

Secondary Outcomes	Pre-Implementation (2022) n=43	Post-Implementation (2023) n=73	p-value
CIWA Score ≥ 24 hours after first recorded CIWA, n (%)			
Mild (0-9)	26 (60.5)	49 (69)	0.35
Moderate (10-15)	1 (2.3)	9 (12.7)	0.09
Severe (≥ 15) *	3 (7.0)	0 (0)	0.05
Unknown/Not recorded	13 (30.2)	13 (18.3)	0.14

*indicates statistically significant difference

CONCLUSIONS

- Average length of stay was significantly increased in the post-implementation group
- Significantly increased use of adjunctive agents, particularly dexmedetomidine, in patients treated with phenobarbital for alcohol withdrawal
- No statistically significant difference in need for mechanical ventilation or ICU admission
- Significantly more patients in the pre-implementation group had a severe CIWA score 24 hours past CIWA treatment initiation
- >20% of post-implementation patients did not require the use of benzodiazepines

LIMITATIONS

- Small retrospective study
- Documentation limitations
- Recent implementation
- Protocol deviations

FUTURE DIRECTIONS

- Provide follow-up education and support on use of phenobarbital for treatment of alcohol withdrawal syndrome
- Examine larger sample size
- Compare separate phenobarbital and benzodiazepine protocols

SELF-ASSESSMENT QUESTION

- Learning Objective: Identify the effects of phenobarbital on average length of stay

What effect did phenobarbital have on average length of stay for patients with a primary diagnosis of alcohol withdrawal syndrome

a) Patients treated with phenobarbital had a decreased length of stay compared to the institution's previous protocol

b) Patients treated with phenobarbital had an increased length of stay compared to the institution's previous protocol

c) Patients treated with phenobarbital had a no change in length of stay compared to the institution's previous protocol

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