

# A Randomized, Prospective, Double Blind Study of Phenobarbital versus Benzodiazepines for Treatment of Alcohol Withdrawal Syndrome

Brandy Snowden, MPH, CCRP, Randy Barnes, MD, Robert A. Dery, MD, Philippe A. Mentler, PharmD and Gregory W. Hendey, MD  
UCSF Fresno Emergency Medicine Program and Community Regional Medical Center, Fresno, CA

## Background/Objectives:

- Lorazepam (Ativan) is commonly used in the ED to treat acute alcohol withdrawal, but its short half-life necessitates adding an oral agent after ED discharge.
- Phenobarbital is also effective, and its long half-life may allow clinicians to omit subsequent oral therapy after ED discharge.
- Our objective was to compare Phenobarbital alone versus Lorazepam plus outpatient oral Chlordiazepoxide (Librium) in the treatment of acute alcohol withdrawal, with regard to symptom amelioration in the ED and after 48 hours, length of ED stay, disposition and rate of return visits.

## Methods:

### Design

Prospective, randomized, double-blind study

### Setting

A Level 1 trauma center Emergency Department with an Emergency Medicine residency program.

### Patient Population

Consenting adults with acute alcohol withdrawal were enrolled over a two year study period.

### Measurements

Symptoms were assessed on a 28 point scale, the modified Clinical Institute Withdrawal Assessment (CIWA) at baseline and 60 minute intervals until discharge or admission, and at 48 hour follow up (see Figure 1).

### Protocol

Patients were randomized to receive Phenobarbital 260mg or Lorazepam 2mg IV, as well as subsequent doses as deemed necessary by the physician.

At discharge, a final CIWA score was recorded, and patients were given either three placebo pills (Phenobarbital group) or three 50 mg Chlordiazepoxide pills (Lorazepam group) for outpatient therapy.

Figure 1. CIWA scale

<b>1. Nausea and Vomiting</b> - Ask "Do you feel sick to your stomach? Have you vomited?"	
Observation	
0- no nausea and no vomiting	
1- mild nausea and no vomiting	
2-	
3-	
4- intermittent nausea with dry heaves	Score: ___(0-7) ___(0-7) ___(0-7) ___(0-7) ___(0-7)
5-	
6-	
7- constant nausea, frequent dry heaves and vomiting	
<b>2. Tremor</b> - Arms extended and fingers spread apart	
Observation	
0- no tremor	
1- not visible, but can be felt fingertip to fingertip	
2-	
3-	
4- moderate, with patients arms extended	Score: ___(0-7) ___(0-7) ___(0-7) ___(0-7) ___(0-7)
5-	
6-	
7- severe, even with arms not extended	
<b>3. Anxiety</b> - Ask "Do you feel nervous?"	
Observation	
0- no anxiety, at ease	
1- mildly anxious	
2-	
3-	
4- moderately anxious, or guarded	Score: ___(0-7) ___(0-7) ___(0-7) ___(0-7) ___(0-7)
5-	
6-	
7- equivalent to acute panic states as seen in severe delirium or acute schizophrenic reactions	
<b>4. Agitation</b>	
Observation	
0- normal activity	
1- somewhat more than normal activity	
2-	
3-	
4- moderately fidgety and restless	Score: ___(0-7) ___(0-7) ___(0-7) ___(0-7) ___(0-7)
5-	
6-	
7- paces back and forth during most of the interview or constantly thrashes about	

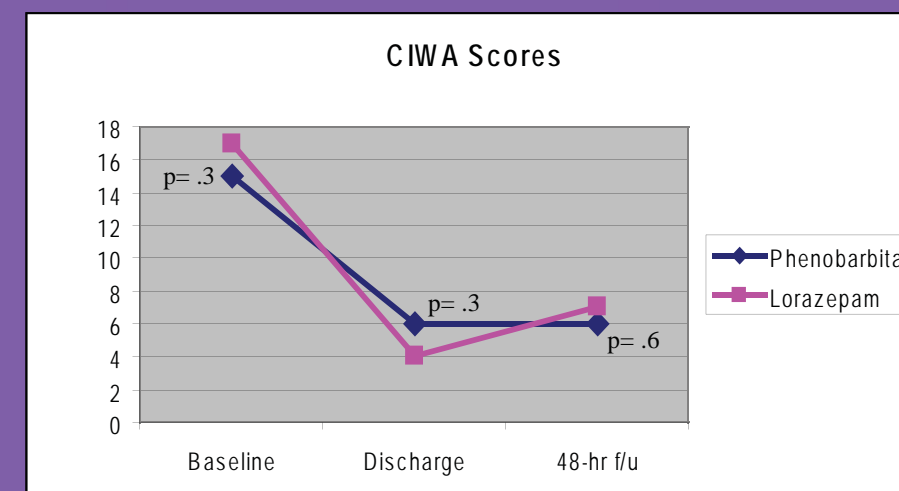
## Results:

- 48 patients were enrolled in the study between 2005 and 2007, and 44 had complete data for analysis.
- 25 received Phenobarbital and 19 Lorazepam. Six patients were admitted (3 from each group) and 18 patients completed follow-up at 48 hours. (Table 1)
- There was no difference in length of ED stay (255 vs. 267 minutes,  $p=.8$ ) or disposition (12% vs 16% admitted,  $p=.8$ ) (Figure 2).

Table 1. Characteristics of study group

	Phenobarbital	Lorazepam	p-value
	N=25	N=19	
Mean age			
Baseline CIWA	15	17	.3
Mean drug dose	509mg	4mg	
Discharge CIWA	6	4	.3
Length of stay	255	267	.8
Admitted	3 (12%)	3 (16%)	.8
Follow-up CIWA	6	7	.6

Figure 2. CIWA scores at baseline, discharge, and 48-hr follow up.



## Limitations:

- Small sample size
- Low proportion of patients who completed 48 hour follow-up.
- Other doses or medications may have been more effective.
- Lack of consecutive enrollment.
- Treatment was not standardized based on CIWA scores.

## Conclusion:

Phenobarbital alone and Lorazepam plus Chlordiazepoxide were similarly effective in the ED treatment of acute alcohol withdrawal, with respect to symptom control, length of stay, treatment failures, and symptoms at 48 hours. We suggest validation with a larger sample size and improved follow up.