

Comparison of Alcohol Withdrawal Outcomes in Patients Treated with Benzodiazepines Alone versus Adjunctive Phenobarbital: a Retrospective Cohort Study

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Background

- Patients with severe alcohol withdrawal or delirium tremens often require high dose benzodiazepines for prolonged periods increasing the risk for over-sedation, mechanical ventilation, and benzodiazepine-induced delirium.
- Phenobarbital is a long-acting barbiturate that has been studied as a benzodiazepine alternative for treatment of withdrawal for planned detoxification and symptomatic control during acute withdrawal syndromes.
- Rapid control using phenobarbital loading doses may reduce risks associated with benzodiazepines and improve symptom management.
- Cumulative phenobarbital dose requirements reported in the literature typically range from 400 to 500 mg.

Research Question

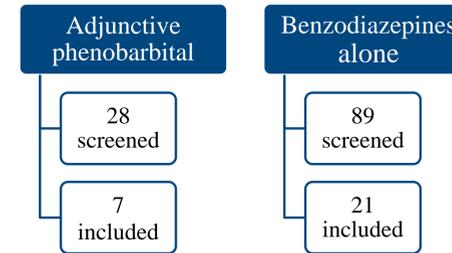
Does the addition of phenobarbital to benzodiazepine therapy improve symptom control and decrease duration of withdrawal when compared to benzodiazepine alone?

Methods

- Retrospective cohort study of patients admitted to an academic medical center
- Subjects were identified through electronic medical record reports for intravenous phenobarbital or intravenous/oral benzodiazepine orders for alcohol withdrawal from March 1st, 2011- October 31st, 2012
- Inclusion criteria: diagnosis of alcohol withdrawal, at least one CIWA-Ar score > 10, received one dose of phenobarbital in the phenobarbital group, and three doses of 20 mg diazepam equivalents within 6 hours in the benzodiazepine group
- Exclusion criteria: ICU admission for initial treatment, positive urine toxicology screen
- The primary endpoint was the proportion of patients with CIWA-AR < 10 at 24 hours from first dose.
- Statistical Analysis: primary endpoint - Fisher's Exact. Differences in duration of withdrawal and cumulative doses were analyzed via Mann-Whitney U

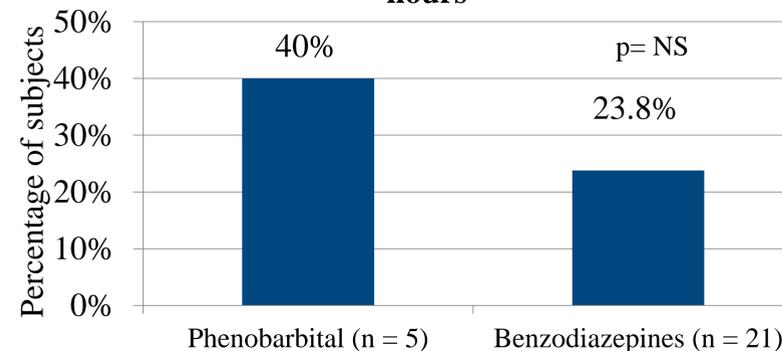
Results

Subject Enrollment and Demographics



	Adjunctive phenobarbital (n = 7)	Benzodiazepines alone (n = 21)
Age [mean (range)]	46.1 (33-58)	49.9 (30-77)
Male [n (%)]	6 (85.7)	18 (85.7)
Prior history of alcohol withdrawal syndromes [n (%)]	4 (57.1)	14 (66.7)

Primary Endpoint: CIWA-Ar < 10 at 24 hours



Secondary Endpoints

	Adjunctive phenobarbital	Benzodiazepines alone	P-value
Duration of withdrawal (hours) Median (IQR)	44 (12-62)	53 (37 – 87)	NS
Cumulative benzodiazepine dose (mg diazepam equivalents) Median (IQR)	25 (20 – 226)	326 (160 – 550)	p = 0.02
Cumulative phenobarbital dose (mg) Median (IQR)	455 (309 – 618)	-	-

Limitations

- Phenobarbital was, in general, administered to patients with more severe withdrawal syndromes which resulted in potential selection bias.
- Inclusion criteria in the benzodiazepine group were selected to minimize this bias.

Conclusions

- Symptom control at 24 hours was not statistically different between groups
- Cumulative diazepam equivalent dose was significantly decreased with adjunctive phenobarbital treatment
- The median phenobarbital dose requirement of 455 mg was similar to previously reported doses.
- Phenobarbital appears to be a safe and effective adjunct to benzodiazepines for the treatment of alcohol withdrawal in non-critically ill patients and may be benzodiazepine sparing.

MEDICINE of THE HIGHEST ORDER

