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

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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.

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 (256 vs. 267 minutes, p=.8) or disposition (12% vs 16% admitted, p=.8) (Figure 2).

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.

Table 1. Characteristics of study group

<table>
<thead>
<tr>
<th></th>
<th>Phenobarbital</th>
<th>Lorazepam</th>
<th>p-value</th>
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</thead>
<tbody>
<tr>
<td>N</td>
<td>25</td>
<td>19</td>
<td></td>
</tr>
<tr>
<td>Mean age</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Baseline CIWA</td>
<td>15</td>
<td>17</td>
<td>.3</td>
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<tr>
<td>Mean drug dose</td>
<td>500mg</td>
<td>450mg</td>
<td>.3</td>
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<tr>
<td>Discharge CIWA</td>
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<td>4</td>
<td>.3</td>
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<tr>
<td>Length of stay</td>
<td>585</td>
<td>467</td>
<td>.8</td>
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<tr>
<td>Admitted</td>
<td>3 (12%)</td>
<td>3 (16%)</td>
<td>.8</td>
</tr>
<tr>
<td>Follow-up CIWA</td>
<td>6</td>
<td>7</td>
<td>.6</td>
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