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A DOUBLE BLIND TRIAL OF GABAPENTIN VS. LORAZEPAM IN THE TREATMENT OF ALCOHOL WITHDRAWAL

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Abstract

Introduction—Some anticonvulsants ameliorate signs and symptoms of alcohol withdrawal, but have an unacceptable side effect burden. Among the advantages of using anticonvulsant agents in this capacity is their purported lack of interaction with alcohol that could increase psychomotor deficits, increase cognitive impairment, or increase intoxication. The aim of the current study was to evaluate alcohol use and symptom reduction of gabapentin as compared to lorazepam in the treatment of alcohol withdrawal in a double-blinded randomized clinical trial.

Methods—One hundred individuals seeking outpatient treatment of alcohol withdrawal with Clinical Institute Withdrawal Assessment for Alcohol-Revised (CIWA-Ar) ratings ≥10 were randomized to double-blind treatment with two doses of gabapentin (900 mg tapering to 600 mg or 1200 tapering to 800 mg) or lorazepam (6 mg tapering to 4 mg) for four days. Severity of alcohol withdrawal was measured by the CIWA-Ar on days 1-4 of treatment and on days 5, 7 and 12 post-treatment and alcohol use monitored by verbal report and breath alcohol levels

Results—CIWA-Ar scores decreased over time in all groups; high-dose gabapentin was statistically superior but clinically similar to lorazepam (p=0.009). During treatment, lorazepam-treated participants had higher probabilities of drinking on the first day of dose decrease (day 2) and the second day off medication (day 6) as compared to gabapentin-treated participants (p=.0002). Post-treatment, gabapentin-treated participants had less probability of drinking during the follow-up post-treatment period (probability=.2 for 900 mg and probability=.3 for 1200mg) compared to the lorazepam-treated participants (probability=.55). The gabapentin groups also had less craving, anxiety, and sedation compared to lorazepam.

Conclusions—Gabapentin was well tolerated and effectively diminished the symptoms of alcohol withdrawal in our population especially at the higher target dose (1200mg) used in this study. Gabapentin reduced the probability of drinking during alcohol withdrawal and in the immediate post-withdrawal week as compared to lorazepam.

Keywords

Gabapentin; Alcohol Dependence; Alcohol Withdrawal; Lorazepam

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INTRODUCTION

Benzodiazepines represent the standard of care for the treatment of alcohol withdrawal and have been shown to prevent alcohol withdrawal seizures and delirium tremens (Mayo-Smith, 1997). However, this class of medications has limitations associated with their use for the outpatient treatment of alcohol withdrawal. First, benzodiazepines have abuse liability (Ciraulo et al., 1998). This is problematic in an outpatient setting. Second, benzodiazepines do blunt cognition which might hamper early attempts at rehabilitation counseling. Third, benzodiazepines have significant interactions with alcohol and opioids. If taken together, there can be additive respiratory depression and cognitive impairment. Lastly, there are some pre-clinical and clinical studies that suggest benzodiazepine use may increase craving and early relapse to alcohol use (Malcolm et al, 2002; Poulos et al., 2004).

Evidence suggests that anticonvulsant agents are also effective in the treatment of alcohol withdrawal (Myrick et al., 2003). Carbamazepine and valproic acid reduce alcohol withdrawal symptoms but have significant side effects that raise safety concerns in patients with alcoholism. Gabapentin is FDA-approved for the management of neuropathic pain syndromes such as postherpetic neuralgia and as an adjunct agent for the treatment of partial seizures. In addition, gabapentinhas been used in the treatment of a variety of psychiatric disorders (Letterman et al., 1999). There is both pre-clinical and clinical evidence suggesting that it may be an effective treatment for alcohol withdrawal (Watson et al., 1997; Myrick et al., 1998; Voris et al., 2003; Mariani et al., 2006). It is not metabolized in the liver, does not bind to plasma proteins or induce hepatic enzymes, has no bone marrow toxicity, is not a scheduled drug, and is eliminated by renal excretion as an unchanged drug (McLean, 1994). While not a scheduled drug, case reports of gabapentin abuse have occurred (Pittenger and Desan, 2007; Victorri-Vigneau et al., 2007). Gabapentin has a moderate side effect profile.

To our knowledge, the current study represents the first double-blind, dose response trial of gabapentin compared to the benzodiazepine lorazepam, commonly used in the outpatient treatment of alcohol withdrawal. The study also was designed to explore gabapentin's potential effects on relapse to drinking in the week after the treatment of alcohol withdrawal based on our group's previous finding that lorazepam-treated participants are at higher risk for post-detoxification drinking as compared to carbamazepine-treated participants (Malcolm et al., 2002).

MATERIALS AND METHODS

Participants

Participants were treatment-seeking patients recruited via newspaper ads and clinical referral. The study setting consisted of an academic medical center in Charleston, South Carolina. Eligibility requirements for study entry included: presence of DSM-IV criteria for alcohol dependence and alcohol withdrawal (First et al., 1997), blood alcohol level 0.1 g/dl or less, Mini-Mental State Exam score ≥26, and admission score on the Clinical Institute Withdrawal Assessment for Alcohol-Revised (CIWA-Ar) ≥10 (Sullivan et al., 1989). Individuals were excluded from participation for the following: all substance use disorders except alcohol dependence, nicotine dependence, or cannabis abuse; major Axis I psychiatric disorder; use of medication in the preceding 30 days that could alter the withdrawal process such as benzodiazepines, beta blockers, calcium channel antagonists, antipsychotics, etc.; history of head injury or other neurological illness including idiopathic epilepsy; medical instability; ECG abnormalities; or grossly abnormal laboratory values (liver enzymes up to three times above normal allowed). Patients who had a history of alcohol withdrawal seizures were included. All participants who met criteria for acceptance into the study signed an Institutional Review Board (IRB) approved informed consent prior

to admission to the study. For ethical reasons, no placebo group was included to avoid withholding effective treatments to outpatients not under the constant supervision afforded by an inpatient setting. This study was registered on the NIH clinical trials database (www.clinicaltrials.gov).

Procedures

Participants were stratified into two groups based on the number of prior medical detoxifications and were randomized to four days of fixed-dose taper of gabapentin or lorazepam. Participants could receive one of three gabapentin dosing regimes: 600 mg (200 mg t.i.d. which was terminated after the first 9 participants-see below), 900 mg (300 mg t.i.d.), or 1200 mg (400 mg t.i.d.) of gabapentin for three days and tapering to 400 mg (200 mg b.i.d.), 600 mg (300 mg b.i.d.), or 800 mg (400 mg b.i.d) on Day 4. Patients randomized to lorazepam could take 6 mg (2 mg t.i.d.) for three days and tapering to 4 mg (2 mg b.i.d.) on Day 4. The gabapentin/lorazepam dosage equivalency was extrapolated from a pilot trial comparing gabapentin to lorazepam in the treatment of alcohol withdrawal (Myrick et al., 2002). In addition, blinded supplemental medications (rescue packs) were given to each participant on Days 1-4 in case additional medications were needed to treat subjective feelings of alcohol withdrawal before the next days scheduled study visit. The gabapentin rescue pack provided two 100 mg doses and one 300 mg dose for use on Day 1. The 300 mg dose was to be reserved for the evening or night use. On Days 2-4 the gabapentin rescue packs provided three 100 mg doses. The lorazepam rescue pack provided two 1 mg doses and one 2 mg dose for use on Day 1. The 2 mg dose was to be reserved for evening or night use. On Days 2-4 the lorazepam rescue packs provided three 1 mg doses. All patients received 100 mg of thiamine orally for 12 days. All medications and rescue packs were assessed at each visit for compliance.

Participants were seen daily on Days 1-5 and again at Day 7 and Day 12. Prior to medication treatment, participants were administered the CIWA-Ar, a validated 10-item scale used to monitor the clinical course of alcohol withdrawal symptoms. The CIWA-Ar total score relates to aggregate alcohol withdrawal severity and rater-assessed individual items include evaluation of nausea, tremor, sweating, anxiety, agitation, perceptual disturbances, and clouding of sensorium. Patients were administered the CIWA-Ar daily by a blinded Masters level research assistant for 4 days at approximately the same time each day during the treatment phase and on Days 5, 7 and 12 (1 day, 2 days and 7 days post-treatment). Breath alcohol levels were measured at each alcohol withdrawal assessment point.

Participants completed the Alcohol Dependent Scale (ADS) (Skiner & Allen, 1982) to quantify the severity of alcohol dependence and the Time-Line Follow-Back (TLFB) (Sobell et al., 1998) to quantify alcohol use during the 14 days prior to study entry as well as daily use during the detoxification treatment phase and during follow-up (Days 5-12). Other measures obtained at baseline, Day 5, Day 7, and Day 12 included the Beck Depression Inventory (BDI) (Beck et al., 1961), the Zung Anxiety Scale (ZAS) (Zung, 1971), the Epworth Sleepiness Scale (EPS) (Johns, 1991), and several visual analog scales to assess craving, ability to perform work, and need for additional medication.

Patients were asked at each visit to rate their global subjective discomfort from withdrawal on a Visual Analog Scale at each visit (0 mm = no discomfort, up to 100 mm = greatest discomfort). Patients were asked to report type and frequency of side effects of treatment medication with each visit. Intensity of side effects and attribution to study medication (not related, possibly related, definitely related) were rated by a blinded Master's level clinician.

The current randomized, double-blind dose response trial tested the hypothesis that gabapentin would be superior to the benzodiazepine lorazepam in the outpatient treatment of

alcohol withdrawal as measured by the CIWA-Ar scale and drinking outcomes as measured by the TLFB and breath alcohol levels. Secondary outcome measures included craving, psychiatric symptoms, and side effects between the treatment groups.

Participants were randomized to treatment groups (doses of gabapentin or lorazepam) using an URN randomization method balancing gender and detoxification history (0-1 vs >1 previous medicated detoxifications) (Stout, 1994). All study personnel and participants were blinded to treatment assignment for the duration of the study. Only the study statisticians and the data safety monitoring committee saw unblinded data, but none had any contact with study participants.

Data Analysis

The primary power analysis was based on a planned comparison of expected CIWA-Ar scores between the medication groups assessed 3 days after the end of treatment (Day 7). This represents the first follow-up data point where there were differential effects between the anticonvulsant carbamazepine and lorazepam in our previous study (Malcolm, et al, 2002). The power was estimated under the assumption of no missing data using a corresponding multivariate analysis for a split-plot design.

CIWA-Ar scores were analyzed as a mixed model (SAS Proc MIXED) with an unstructured variance/covariance matrix. Scores across the treatment and follow-up periods were conditioned on the baseline CIWA-Ar scores and drinks per day from the TLFB over the immediately preceding 14 days. Simple effects were examined in the case of significant interactions. This analysis is robust in the face of non-informative missing data.

The pattern of relapse drinking (dichotomous variable: drink vs. no drink) across individual days was analyzed using a generalized estimating equations analysis (GEE) for repeated measure logistic regression (SAS: Proc Glimmix). Briefly, this analysis accounts for the fact that observations within an individual are more closely related to other observations with the same individual than observations between individuals in much the same way as repeated measures ANOVA or a Mixed Model. The between subject variable was group (the two gabapentin doses and lorazepam) and day (days 1 through 12 from the time-line follow-back). Group differences in the temporal pattern of drinking across days is indicated by a significant group by day interaction.

Drinking Outcomes—Drinking was assessed by the breath alcohol and TLFB over the 12 days of the study and analyzed as a binary outcome (drink vs. abstinent) in the treatment and follow-up periods. A Generalized Estimating equation approach was used for the mixed model categorical analysis (HLM 6.0) analogously with the secondary continuous variables (below). Drug Groups and experimental period were indicator coded and main effect or interactions tested as joint contrasts of the appropriate dummy variable coefficients.

Secondary Outcome Variables—Since the design had the two primary observation phases, treatment and follow-up, we also examined the overall group effects during the two phases in a nested design (days nested within phase). Planned simple contrasts were used, i.e. low dose and high dose gabapentin vs lorazepam in each of the two phases of the experiment. This analysis was also done in the context of a mixed model.

Covariates—In addition to the primary analysis of CIWA-Ar scores above, several variables were assessed as covariates to control for various potential confounds and potentially reduce error variance in the model. Pre-treatment drinks per day and ADS score were assessed as constant covariates in the analysis. Both explained significant variance.

Drinks per day was employed in the final analysis since it remained significant when both were added to the model, whereas ADS score did not.

RESULTS

Retention and Completion

Age-eligible participants were recruited from January, 2001 to May, 2005. Of the 281 individuals evaluated for study participation, 100 participants signed informed consent and were randomized to treatment. Seventy-four completed four days of detoxification treatment of which 68 completed post-detoxification follow-up appointments at Day 5, Day 7 and Day 12. There was no differential drop-out rate between treatment groups (p=.42).

The lowest dose (600 mg/day) gabapentin group (n=16) was discontinued after two patients reported medically unwitnessed seizure-like episodes and one subject had a near-syncopal event. The data from these participants were not included in the analysis. As such, during the remainder of the text, high dose refers to the gabapentin 1200 mg groups and low dose refers to the gabapentin 900 mg group.

Baseline Characteristics

As can be seen in Table 1 there were generally no significant differences in demographics between gabapentin and lorazepam-treated groups. High dose gabapentin subjects were ingesting about five drinks per day more than the other groups (p=.041).

Medication Dosing

Supplemental rescue medications increased the daily amount of medication taken in all groups. However, there were no significant differences in the number of rescue doses needed between groups (p=.75). The mean dose of the gabapentin for those assigned to the target 1200 mg group was 1423, 1145, 1160, and 860 mg/day for Days 1-4 respectively. The mean dose of gabapentin for those assigned to the target 900 mg group was 1118, 981, 973, and 689 mg/day for Days 1-4 respectively. The mean dose of lorazepam was 7.6, 7.3, 7.0, and 5.3 mg/day for Days 1-4 respectively.

Alcohol Withdrawal Symptoms

CIWA-Ar scores, as expected, decreased systematically with time (Figure 1) in all groups. The declining pattern was similar over the first 4 (medication) days, though the high dose gabapentin resulted in lower scores than either the lorazepam group or the low dose gabapentin group. The latter two did not differ from each other. The lower CIWA-Ar scores were especially striking following the discontinuation of medication. CIWA-Ar scores in the high dose gabapentin participants continued on the decreasing trajectory, while the other two groups diverged, particularly on Day 7 where CIWA-Ar scores stayed higher most notably in the lorazepam-treated participants. The mixed model analysis was consistent with these observations in that a strong main effect of drug group was detected. Simple contrasts revealed that the high dose gabapentin group (p=.009), but not the low dose gabapentin group (p=.62), had significantly lower CIWA-Ar scores than the lorazepam group, overall. A group by day interaction (p=.013) was found and was primarily the result of the divergence in CIWA-Ar scores between groups immediately after the drug was discontinued. Follow-up analysis using the nested model contrasts revealed a significant difference between the high dose gabapentin group and the lorazepam group during both the treatment and follow-up phases of the experiment (p=.03 and p=.006, respectively; see Table 2). The drug by phase analysis was suggestive of an interaction, but did not reach significance (p=0.18).

An ordinal mixed model (HLM 6.0) showed a significant drug by day interaction (X^2 (7) = 19.6, p=007) (high dose gabapentin reducing CIWA-Ar scores more than lorazepam), due primarily to the last two, post-treatment follow-up observations. A similar analysis with time as a continuous variable revealed a significant effect of drug (high dose gabapentin reducing CIWA-Ar scores more than lorazepam) on the decline in ratings over time with no difference in intercept.

Drinking During and After Treatment

A distinctly different pattern across days was observed in the lorazepam vs. gabapentin treated individuals (Group by Day interaction, f(1,734)=3.24, p=.0002). On the initial day of medication, gabapentin participants were more likely to drink than lorazepam subjects. Drinking on gabapentin declined across the treatment days and then increased modestly and slowly over the post-medication period. Lorazepam participants, although virtually abstinent on the first medication day, increased probability of drinking thereafter, showing peaks at Day 2 (first dose reduction) and particularly on Day 6, the second post-medication day.

Figure 2 shows the probability of drinking on each day for the two groups as estimated by the GEE model. Drinking at the two doses of gabapentin was indistinguishable (Main effect of dose: f(1,427)=.07,p=.79, Dose by Day interaction f(11,427=1.27,p=.24). Group differences between gabapentin-treated participants and lorazepam-treated participants were marginally significant at day 1 (t(734)=1.79, p=.07) and were significant at days 2, 3 and 6 (p=.027, .019 and .0009, respectively).

Secondary Variables

Contrasts of lorazepam vs. the two doses of gabapentin are reported in Table 2. Craving was significantly reduced relative to lorazepam in both gabapentin doses during the medication period, while there were no differences among the groups during the follow-up phase. Gabapentin participants, at both doses, scored significantly lower on the Zung Anxiety scale than did lorazepam participants during the medication period. This was the case also during the follow-up period for the high dose, but not the low dose, of gabapentin. The Beck Depression Inventory was significantly lower in the low dose gabapentin group than in the lorazepam group during the medication period. The Epworth Sleepiness scale was significantly lower in the high dose gabapentin vs lorazepam group during the medication, but not during follow-up. The only significant result among the four visual analog scales was that high dose gabapentin participants rated their ability to perform work better than lorazepam participants during follow-up. This was not true of the low dose gabapentin group.

Side Effects

Overall, there was no difference in self-reported side effects between participants treated with gabapentin versus lorazepam (p=.74). There was a tendency for lorazepam participants to report more sedation (p=.12). There was a tendency in the gabapentin participants to report more intoxication (p=.17) and more pruritis (p=.17). One gabapentin participant was withdrawn due to rash and urticaria, treated with diphenhydramine. Two participants in the discontinued 600 mg gabapentin group had probable single withdrawal seizures and one had a syncopal event. This dosage group was stopped upon recommendation of our Data Safety Monitoring Board after review of these cases. No patients experienced delirium tremens in any treatment group.

DISCUSSION

Results of this study indicate that the anticonvulsaant gabapentin, as measured by CIWA-Ar scores, was as at least as effective as the benzodiazepine lorazepam in the outpatient treatment of alcohol withdrawal at the doses used in this study. The high dose gabapentin (1200 mg) was found to be of marginal clinical but of statistical superiority to both lorazepam and low dose gabapentin (900 mg) in decreasing alcohol withdrawal symptoms.

Participants treated with either high dose (1200 mg) or low dose (900 mg) of the anticonvulsant gabapentin had lower odds of drinking alcohol both during treatment and in the week post treatment. Those treated with high dose gabapentin had less anxiety and rated their ability to perform work higher than lorazepam-treated subjects. During the medication treatment phase of the study, participants treated with high dose gabapentin had less craving for alcohol, less anxiety, and less daytime sedation as compared to participants treated with lorazepam. During the same treatment phase, participants treated with low dose gabapentin had less craving for alcohol and less anxiety, but also less depressive symptoms.

Although it is unclear how gabapentin exerts its pharmacological effects, it has been shown to bind with high affinity to auxiliary alpha(2)delta subunits (specifically the alpha(2)delta-1 and alpha(2)delta-2 subtypes) of voltage-gated calcium channels (Davies et al., 2007; Gee et al., 1996), which results in a plethora of down-stream neurochemical alterations. Nevertheless, from a mechanistic point of view, there is rationale to support the use of gabapentin during acute alcohol withdrawal. Gabapentin has been found to potentiate CNS GABA in humans (Petroff et al., 1996), inhibit glutamate synthesis, modulate calcium current, inhibit sodium channels, and reduce norepinephrine and dopamine release (Cho et al., 1998; Taylor, 1998). Gabapentin's unique pharmacology of increasing GABAergic tone and reducing glutamatergic tone in the brain should reverse the low GABA/high glutamate state found after cessation of drinking (Littleton, 1998). This implies that gabapentin should be a useful therapeutic agent in normalizing the hyperactive state of the brain that is characteristic of alcohol withdrawal. In addition, the potential neuroprotective actions of gabapentin may decrease the neurotoxic effects associated with alcohol withdrawal (Baydas et al., 2005).

There are several possible reasons why gabapentin decreased drinking during alcohol withdrawal treatment as compared to placebo. It is established that 30-50% of alcoholics relapse during the first three months after stopping drinking (Mann et al., 2004; Kyrstal et al., 2001). This vulnerable period to relapse is associated with impaired sleep, mood instability, and anxiety. These symptoms are suggested to play a role in relapse to alcohol use (Littleton, 1998). In the current study, gabapentin reduced craving, anxiety/depressive symptoms and individuals complained of less subjective discomfort as compared to the individuals treated with lorazepam. As such, gabapentin may have blocked these important triggers to continue alcohol consumption. Whether gabapentin has an effect on reinforcement mechanisms separate from reducing neurotransmitter abnormalities associated with alcohol withdrawal is not known. However, individuals treated with gabapentin did endorse less craving for alcohol during treatment than did lorazepam-treated individuals, but this craving may have been related to early abstinence or alcohol withdrawal effects leading to an urge for relief drinking. It has been postulated that agents that affect GABA/glutamate balance might also be useful in relapse prevention, especially during the early stages of abstinence where perturbations in these systems might underlie craving and relapse (Littleton, 1998; Anton, 1999). In fact, other studies have been suggested gabapentin to be useful in preventing relapse and reducing drinking (Bisaga et al., 2006 Furieri et al., 2007; Brower et al., 2008). Gabapentin has been found to decrease stimulated dopamine release in striatal and limbic areas thought to be associated with drug-induced relapse (Pugsley et al.,

1998). As such, gabapentin may have an effect on reinforcement mechanisms which is independent of its effects on acute or protracted withdrawal symptoms.

From a safety and tolerability standpoint, both drugs were similar. While several anticonvulsant agents have been found effective in the treatment of alcohol withdrawal, some of these agents have side effects or complications that may cause concern when used in alcoholics. These complications include liver toxicity, thrombocytopenia, pancreatitis and bone marrow toxicity. Gabapentin is free of such side effects and may be safer than carbamazepine or valproic acid, but no comparison trials have been made. In addition, due to a saturable transport mechanism in the gut, gabapentin has been found to be safe in overdose. Of the six reported overdose cases in the literature, two have documented elevated gabapentin concentrations and lack of serious clinical toxicity (Fernandez et al., 1996; Garofalo et al., 1993). Of importance to the use of gabapentin in alcoholism, one case report documented an ingestion of 91 grams of gabapentin with large amounts of beer and whiskey without serious side effects (Fernandez et al., 1996). Recent work by our group suggested that gabapentin did not interact negatively with alcohol under controlled conditions (Myrick et al., 2007).

Initially, the intent of the study was to compare three doses of gabapentin to lorazepam: 600mg, 900mg, and 1200mg. The gabapentin 600mg dose was discontinued after three significant adverse events occurred. As noted above, two individuals experienced seizure-like activity during treatment, and one individual had a syncopal episode requiring emergency room assessment, indicating that this dose was ineffectively low. None of these events were observed in the two higher dose groups in this study. Nevertheless, the fact that all three occurred in the lowest gabapentin group suggests that the population under treatment was indeed vulnerable to more severe alcohol withdrawal symptoms and that the medications used in the other groups likely inhibited the more severe alcohol withdrawal symptoms from being expressed.

There are several limitations in the current study. Participants that were selected had extensive drinking histories, but with only mild to moderate withdrawal severity. Many of our participants were in better general health than patients in alcohol withdrawal presenting to emergency departments or hospitals. Although we had a benzodiazepine index group, we did not have a placebo group for ethical reasons. Thus, it is not possible to make absolute comparisons between drugs and the natural course of untreated withdrawal. Gabapentin and many other anticonvulsants are not available for parenteral administration and are inappropriate in vomiting or uncooperative delirious patients. Our sample size was relatively small and conclusions about side effects of uncommon frequency cannot be made. One can argue that a different dosing schedule of lorazepam or a different benzodiazepine might have yielded different results. The resources to evaluate such questions are however substantial and can only be definitely determined in a large multi-dosing multi-center trial.

In conclusion, the current study adds to a growing literature on the use of gabapentin in alcoholism. Specifically, gabapentin was found to be superior to the benzodiazepine lorazepam in the treatment of outpatients in moderate alcohol withdrawal as measured by lower probability of drinking and by superior but clinically similar alcohol withdrawal symptom reduction. Rarely has drinking during detoxification been examined in alcohol withdrawal treatment trials, so our data provide important new information on this important issue. Studies enrolling individuals with more severe alcohol withdrawal symptoms and medical comorbidities are needed to provide further evidence of the utility of gabapentin in the treatment of more complicated withdrawal symptoms.

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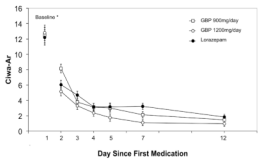

Figure 1.

Alcohol withdrawal symptoms: CIWA - Ar score over time.
Comparisons: GBP 900mg vs 1200mg: t = 5.83, p = 0.019
GBP 900mg vs Lorazepam: Not significant
GBP 1200mg vs Lorazepam: t = 6.86, p = 0.011
* Baseline CIWA-Ar score used as a covariate in the analysis

Figure 2.
Probability of drinking during treatment and follow-up.

Table 1

Demographics of study population. No significant differences between treatment groups except where indicated. Standard error is in parentheses

	Gabapentin 900mg (n=28)	Gabapentin 1200mg (n=28)	Lorazepam (n=28)
Gender (% male)	70%	91%	70%
Age (years)	38.4 (1.82)	40.5 (2.25)	39.1 (1.83)
Education (years)	13.3 (.605)	13.8 (.679)	13.1 (.299)
Income per month	$1018.20 (294.9)	$1154.30 (244.1)	$1730.90 (283.12)
ADS Total Score	23.1 (1.55)	22.0 (1.55)	25.7 (1.55)
Years of Alcohol Use	17.4 (2.04)	23.45 (2.30)	23.78 (1.75)
Years of Alcohol Use to Intoxication	11.6 (2.36)	14.73 (2.12)	13.52 (1.58)
Drinks Per Day (prior 14 days)	12.1 (1.16)	16.8 (2.18)*	11.4 (1.11)

*Gabapentin 1200mg group higher than other groups (F = 3.38, p=.041)

Table 2

Clinical parameters during and after alcohol detoxification. Standard error is in parentheses

	Medication Phase			Follow-up Phase		
	GBP 900mg	**GBP 1200mg**	**Lorazepam**	**GBP 900mg**	**GBP 1200mg**	**Lorazepam**
CIWA-Ar[a]	4.52(39)	3.14(.37)*	4.26(.38)	1.79 (.32)	1.03(.31)**	2.53(.31)
Alcohol Craving (Range 0-100)	29.19(5.0)*	28.73(4.6)*	42.7(4.7)	13.9(5.3)	20.4(4.8)	20.8(4.9)
Zung Anxiety Scale	32.11(1.74)*	31.89(1.6)*	36.98(1.5)	31.25(1.3)	28.8(1.2)**	33.9(1.2)
Beck Depression Inventory	6.8(.57)**	9.5(1.2)	11.6(1.2)	5.3(1.4)	7.2(1.3)	7.2(1.2)
Epworth Sleepiness Scale	6.48(.57)	5.74(.52)*	7.38(.53)	5.12(.7)	5.29(.67)	6.26(.67)
Subjective Discomfort[b] (range 0-9)	3.82(.35)	3.91(.33)	3.97(.33)	2.57(.38)	2.41(.35)	2.90(.36)
Quality of Sleep[b] (range 0-9)	5.17(.49)	3.96(.44)	5.14(.45)	4.18(.61)	5.04(.56)	4.80(.57)
Ability to perform work[b] (range 0-9)	4.78(.52)	4.04(.46)	5.11(.46)	3.46(.84)	2.47(.75)*	4.83(.74)
Need for additional medication[b] (range 0-9)	4.05(.51)	3.39(.44)	4.22(.44)	3.16(.65)	2.31(.57)	3.17(.56)

Statistics represent contrasts with lorazepam:

* < 0.05

** < 0.01

[a] Mean CIWA-Ar score over the 5 day medication period.

[b] Mean rating on 0 - 9 visual analog scale during the 5 day medication period