

Admission Alcohol Level: A Predictor of the Course of Alcohol Withdrawal

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Background. Little is known about how to predict the course of alcohol withdrawal. This study explores relationships between alcohol levels at admission to a detoxification unit and the severity and outcome of alcohol withdrawal.

Methods. A retrospective cohort study was conducted in two institutions, the Mid-Missouri Mental Health Center (MMMHC) and the Harry S Truman Memorial Veterans Hospital (HSTMVH), of individuals admitted during 1 year.

Results. The alcohol levels at admission of the 86 clients at the Mental Health Center and the 99 patients at the HSTMVH, correlated with withdrawal severity

over the first 48 hours after admission ($R^2 = .26$ at MMMHC, $.41$ at HSTMVH, $P < .0001$ for both), and remained significantly associated even after adjustment for other variables. Furthermore, individuals who had lower alcohol levels at the time of admission were more likely to stay for rehabilitation following detoxification ($P < .001$ for both institutions).

Conclusions. A patient's alcohol level at the time of admission to a detoxification unit may help predict the severity of withdrawal and the treatment outcome.

Key words. Substance withdrawal syndrome; alcoholic intoxication; alcoholism, rehabilitation.
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Few studies have explored for correlations between variables present at admission to an alcohol detoxification and treatment program and either the severity of alcohol withdrawal or the outcome of therapy. An ability to predict the likely course of alcohol withdrawal is important for a number of reasons.

First, many individuals receive treatment for alcohol withdrawal in nonmedical facilities. According to the National Drug and Alcoholism Treatment Unit Survey in 1987,¹ 43% of persons who went through inpatient detoxification were in nonmedical units. While most such persons do well without pharmacological treatment of their withdrawal, some develop medical problems, some of which require urgent transfer of the patient to a medical facility. The ability to predict which clients might have such difficulties would be clinically useful.

Second, some patients currently admitted to medical detoxification facilities could probably be managed effectively in nonmedical settings. If variables measurable on initial evaluation could reliably identify those who do not

need medical therapy, treatment could be provided at less cost and with no compromise in quality.

Third, being able to predict the course of withdrawal could help focus research efforts by guiding the selection of patients for study, identifying potential confounding variables, and clarifying to whom the results can be generalized.

Past studies in this area have shown conflicting results. Shaw and her colleagues² followed the progress of 38 hospitalized patients by repeatedly measuring withdrawal severity using their Clinical Institute Withdrawal Assessment for Alcohol scoring system. Surprisingly, the 28 patients whose withdrawal was milder and who responded to nondrug treatment had a history of more alcohol consumption over more years than those whose withdrawal was more severe, requiring pharmacotherapy. Although details were not given in their report, they noted that serum levels of liver enzymes were higher in the patients who failed nondrug therapy, suggesting that those may be of value in predicting the course of withdrawal.

Pristach and her associates³ studied associations between a carefully collected history of recent alcohol consumption and the severity of withdrawal in a series of 43 patients admitted to a medical detoxification unit. They found a significant correlation between the amount of

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alcohol consumed over the 7 days before admission and the severity of withdrawal. Although they measured alcohol levels at admission, they did not examine possible correlations between those levels and withdrawal severity.

Clothier and his co-workers⁴ studied the rate of alcohol clearance in 15 patients admitted for medical therapy of withdrawal, and found no correlation between alcohol clearance rate and the amount of chlordiazepoxide used. They did find an association between the initial blood alcohol level and the amount of medication required during treatment, but did not report a correlation coefficient. They concluded, however, "Neither the metabolic rate nor the initial blood alcohol level provided the clinician any indication of the severity of withdrawal symptomatology or amount of medication that was required."⁴

Gorelick and Wilkins⁵ stated in their review of the literature that severity of alcohol withdrawal in animals closely correlates with the amount and duration of alcohol consumption, but in humans only about one third of the differences in severity is accounted for by these variables. They concluded that research into alcohol withdrawal should consider several questions, the first of which is, "Are there specific, measurable factors that predict the severity of acute withdrawal, so that individual patients can be more confidently assigned to medical vs social detoxification programs?"⁵

Castaneda and Cushman⁶ agreed in their 1989 review, calling our ability to predict the severity of alcohol withdrawal "a vastly underresearched area in alcoholism."

The present research study was undertaken to explore characteristics measured at admission, particularly alcohol level, as predictors of the severity and outcome of alcohol withdrawal.

Methods

A retrospective cohort study was carried out in two institutions, the Mid-Missouri Mental Health Center's alcohol- and drug-addiction treatment unit (MMMHC) and the Harry S Truman Memorial Veterans Hospital (HSTMVH). A computer-generated chronological list of all patients admitted to the HSTMVH during the year October 1988 through September 1989 was divided into blocks of 25 names, and alternate blocks were chosen for review. After excluding missing charts, a systematic sample of 114 of the 220 patients remained. Charts of all individuals admitted to MMMHC during the same year were reviewed.

The MMMHC unit is a nonmedical, social detoxi-

fication setting, staffed primarily by alcoholism counselors. Clients whose withdrawal symptoms are judged to be too severe for successful nondrug detoxification and those who develop seizures are transferred to the University of Missouri-Columbia Hospital for medical treatment. The HSTMVH operates a medical detoxification unit, and uses a protocol of chlordiazepoxide in the management of alcohol withdrawal. All admissions to the HSTMVH unit are voluntary. All patients have the opportunity to stay on the units for alcoholism therapy following withdrawal and are encouraged to do so.

Data were collected by chart review and included age and sex. Estimates of the amount of alcohol (in grams of ethanol) consumed per day were calculated based on data from the admission nursing assessment records, assuming alcohol contents of 20.5 g per 12-ounce beer, 90 g per fifth of wine, and 300 g per fifth of liquor. Duration of alcohol problems (in years), months of daily drinking, concurrent medications, and illicit drugs used were also taken from the admission notes. Alcohol level at the time of admission (breath alcohol at MMMHC, blood alcohol at the HSTMVH) and various laboratory values were taken from the laboratory records in the chart. Breath alcohol levels at MMMHC are determined by an Alco-Sensor III (Intoximeters Inc, St Louis, Mo), which correlate well with blood alcohol levels ($r = .879$).⁷ Withdrawal severity assessment scores at MMMHC and amount of chlordiazepoxide used at the HSTMVH were taken from flow charts in the medical records. Whether the patient or client left the unit or (at MMMHC) required transfer for medical detoxification before the end of the 7th day was used to determine, for the purposes of this study, the disposition at the end of the detoxification period.

At MMMHC, withdrawal symptoms were scored every 2 to 4 hours, usually throughout the first 48 hours of the client's stay. Tremor, sweating, nausea and vomiting, agitation, sleeplessness, confusion, hallucinations, tachycardia, hypertension, and fever were each scored 0 to 3, and the resultant 10 scores are summed to give a severity assessment score. A score over 6 is considered an indication for a medical consultation to consider transferring the patient to a medical detoxification center. The occurrence of convulsions is noted. To assess the severity of withdrawal at MMMHC for the purposes of this study, the area under a curve plotting withdrawal assessment scores vs time was calculated for each client by multiplying the score at a given time by the number of hours until the next assessment, and summing those products over the first 48 hours. For an example of such a graph, see Figure 1.

At the HSTMVH, 50 mg of chlordiazepoxide is given orally, every hour if necessary, if the patient has a

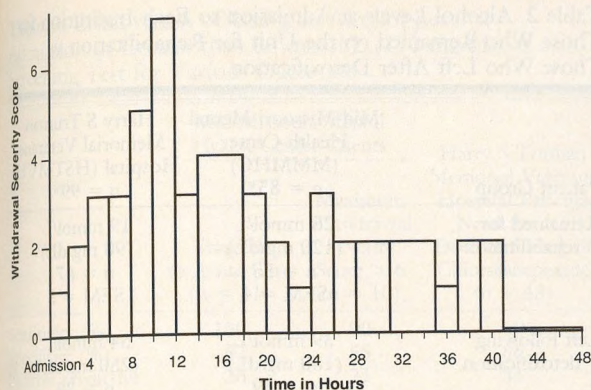


Figure 1. An example of a patient's withdrawal assessment scores during the first 48 hours of detoxification. Each withdrawal symptom (tremor, sweating, nausea and vomiting, agitation, sleeplessness, confusion, hallucinations, tachycardia, hypertension, and fever) was given a score of 0 to 3 and the total added to determine the severity level as indicated on the Y-axis. Scores were determined every 2 to 4 hours. For the purposes of this study, each score was multiplied by the number of hours until the next assessment was done (since the scores were obtained at different intervals), and those products were added. The total, 110 in this case, is the sum of the areas of the rectangles that make up this graph.

20 mm Hg orthostatic drop in systolic blood pressure or a 20-point increase in pulse, a fever greater than 37°C (99°F), hallucinations, tremor, or notable irritability. The total amount of chlordiazepoxide used in the first 48 hours was taken as the primary measure of the severity of withdrawal for the purposes of this study.

Data were analyzed using *t* tests and one-way analysis of variance to compare means of groups, and multiple regression to examine the effect of admission alcohol level on measures of the severity of withdrawal, controlling for other variables. In comparing an ordinal variable with an interval-level variable, both analysis of variance and linear regression were used.

This research was approved by the Institutional Review Board of the University of Missouri-Columbia School of Medicine, by the administrative staff of the MMMHC, and by the administrative staff of the HSTMVH.

Results

At MMMHC, 119 cases were reviewed (99 men and 20 women). The average age of the clients was 37 years (SD ± 12.3). Among the 115 clients for whom an estimated daily alcohol consumption was recorded, the mean amount was 377 g/d (SD ± 251).

At HSTMVH, 114 charts were reviewed, all of

them charts of men, whose average age was 45 years (SD ± 11.3). Daily alcohol consumption was recorded for 103 of them, with a mean of 361 g/d (SD ± 183).

At MMMHC, the 48-hour score-by-time approximation of the area under the withdrawal-severity-score curve averaged 65 (SD ± 51). At HSTMVH, the amount of chlordiazepoxide used in the first 48 hours averaged 133 mg (SD ± 186).

Alcohol levels were determined in 86 (72%) of the MMMHC clients (mean of 37 mmol/L [170 mg/dL], SD ± 28) and in 99 (87%) of the HSTMVH patients (mean of 30 mmol/L [140 mg/dL], SD ± 33). At MMMHC, those who had an alcohol level measured were older than those who did not (38 years compared with 33 years, $P = .03$), but this difference was not found with the HSTMVH patients. At HSTMVH, patients who had an alcohol level measured received more chlordiazepoxide in the first 48 hours (149 mg) than those whose levels were not determined (24 mg, $P = .02$), but at MMMHC the withdrawal severity scores were not significantly different for those who had an alcohol level measured compared with those who did not. In the following analyses, only those individuals who had an alcohol level determined are included.

For the MMMHC clients, linear regression analysis demonstrated a significant relationship between breath alcohol level at admission and the area under the withdrawal-score curve ($P < .0001$). The amount of variance explained, R^2 , was .26. When aspartate aminotransferase (AST) was then entered into the equation, R^2 increased to .41 (with $P < .0001$), and the association between breath alcohol level and the score-time product was still statistically significant ($P = .002$). By itself AST was also associated with severity of withdrawal ($R^2 = .23$, $P < .0001$). Entering age, sex, use of illicit drugs, and the presence or absence of other medical illness did not change the magnitude or statistical significance of the relationship between alcohol level and withdrawal severity. Estimates of the amount and duration of alcohol use showed no significant correlation with the severity of withdrawal when entered into multiple regression equations with or without alcohol level.

In the HSTMVH data, regression analysis showed an association between alcohol level at admission and severity of withdrawal, as measured by the amount of chlordiazepoxide used in the first 48 hours, with an R^2 of .41 ($P < .0001$). With AST added to the equation, R^2 increased slightly to .44, and the association between alcohol level and the amount of chlordiazepoxide used remained significant ($P < .0001$). AST by itself was also correlated with the amount of medication used ($R^2 = .09$, $P = .002$). Patient age was not correlated with the amount of chlordiazepoxide used. By itself, the estimate

Table 1. Mean Alcohol Levels at Admission to the Two Institutions and the Patients' Maximal Severity of Tremor During Withdrawal

Severity of Tremor (score)	Mid-Missouri Mental Health Center n = 85*	Harry S Truman Memorial Veterans Hospital n = 95*
None (0)	22 mmol/L (100 mg/dL) n = 27, SEM 4	12 mmol/L (50 mg/dL) n = 44, SEM 3
Mild (1)	35 mmol/L (160 mg/dL) n = 29, SEM 5	29 mmol/L (140 mg/dL) n = 19, SEM 7
Moderate (2)	54 mmol/L (250 mg/dL) n = 24, SEM 6	50 mmol/L (230 mg/dL) n = 23, SEM 7
Severe (3)	49 mmol/L (230 mg/dL) n = 5, SEM 15	60 mmol/L (280 mg/dL) n = 9, SEM 9
	P = .0002†	P < .0001‡

*Number of patients does not equal total number who had an alcohol level determined (86 at MMMHC, 99 at HSTMVH) because of missing data.

†By analysis of variance.

of the number of years of drinking problems correlated weakly with the severity of withdrawal ($R^2 = .07$, $P = .04$), but was no longer statistically significant when the alcohol level was included in the equation. Estimates of the amount of alcohol consumed showed no correlation with the amount of chlordiazepoxide used.

In data from both institutions, the association between alcohol level at admission and severity of withdrawal changed little and remained statistically significant when those with a level of zero (15 clients at MMMHC and 43 at the HSTMVH) were omitted from analyses ($P = .001$ with the data from MMMHC, $.004$ in the HSTMVH data).

Since Shaw and her associates² indicated that vital signs are not an accurate measure of the severity of alcohol withdrawal, we also looked for a possible association between the maximum severity of tremor (scored 0 to 3 in both institutions) and the alcohol level at admission. As shown in Table 1, a statistically significant relationship was found, both by one-way analysis of variance ($P = .0002$ at MMMHC, $<.0001$ at the HSTMVH) and by multiple regression (with $R^2 = .19$ with the MMMHC data and $.32$ with the HSTMVH data, $P < .0001$ in both). Statistically, the slopes of the regression lines in the two sets of data were not significantly different.

In data from both institutions, alcohol levels at admission were lower among those who stayed on the unit for rehabilitation following the initial withdrawal

Table 2. Alcohol Levels at Admission to Each Institution for Those Who Remained on the Unit for Rehabilitation vs Those Who Left After Detoxification

Patient Group	Mid-Missouri Mental Health Center (MMMHC) n = 85*	Harry S Truman Memorial Veterans Hospital (HSTMVH) n = 99*
Remained for rehabilitation	26 mmol/L (120 mg/dL) n = 35 SEM = 4	19 mmol/L (90 mg/dL) n = 67 SEM = 3
Left following detoxification	39 mmol/L (180 mg/dL) n = 39 SEM = 4	54 mmol/L (250 mg/dL) n = 32 SEM = 5
Transferred for medical detoxification (MMMHC only)	67 mmol/L (310 mg/dL) n = 11 SEM = 7	N/A
	P < .0001†	P < .001‡

*Number of patients does not equal total number who had an alcohol level determined (86 at MMMHC, 99 at HSTMVH) because of missing data.

†By analysis of variance.

‡By t test.

period (Table 2). The differences within each institution are statistically significant, with $P < .0001$ for MMMHC by analysis of variance (the third group being those transferred for medical detoxification) and $<.001$ for the HSTMVH by t test.

Eleven of the 119 MMMHC clients were transferred to the University of Missouri-Columbia Hospital for medical detoxification. All had an alcohol level determined at admission, with a mean of 67 mmol/L (310 mg/dL) (SD ± 23), significantly higher ($P < .05$ by analysis of variance with Tukey's multiple range test) than the mean level in clients not transferred (Table 2).

When the MMMHC clients were classified into two groups based on the median level of alcohol at admission (≤ 33 mmol/L [150 mg/dL] or >33 mmol/L), high alcohol levels were associated with several adverse outcomes, including transfer to the acute care hospital for medical detoxification and a maximum withdrawal assessment score of greater than 6 (the level the staff there uses to indicate that a medical consultation is necessary). When applied to the HSTMVH data, the same alcohol-level threshold effectively distinguished between those patients who required a total of 50 mg of chlordiazepoxide or less and those who required more.

Among the MMMHC clients, nine of the ten who had a maximal withdrawal assessment score over 6 had an alcohol level at admission of over 33 mmol/L (150 mg/dL), a sensitivity of 90%. Of the 75 with maximal withdrawal scores below 7, 41 had an alcohol level at admission of less than 33 mmol/L (150 mg/dL), a specificity of

Table 3. Effectiveness of Using an Alcohol Level at Admission of Greater than 33 mmol/L (150 mg/dL) as a Screening Test for Various Outcomes

	Mid-Missouri Mental Health Center Clients		Harry S Truman Memorial Veterans Hospital Patients Need for >1 Dose of 50 mg of Chlordiazepoxide (n = 43)
	Transfer to Acute Care (n = 11)	Maximum Withdrawal Severity Score > 6 (n = 10)	
Sensitivity (%)	100	90	69
Specificity (%)	57	55	86
Positive predictive value (%)	26	21	81
Negative predictive value (%)	100	98	77

In each column, n equals the number of patients who had that outcome.

55%. The positive predictive value of a cutoff alcohol level of 33 mmol/L (150 mg/dL) for this particular adverse outcome was only 21%. Of the 42 with an alcohol level below 33 mmol/L (150 mg/dL) at admission, only one had a maximal withdrawal score over 6, giving a negative predictive value of 98%. Similar calculations were used to generate the other sensitivities and specificities given in Table 3.

Using higher or lower alcohol levels (between 22 and 43 mmol/L [100 and 200 mg/dL], respectively) as the threshold was less effective in separating these groups, with minimal increases in sensitivity (or specificity) accompanied by decreases in specificity (or sensitivity).

Among the patients studied, 13 at HSTMVH and 17 at MMMHC had a history of one or more withdrawal seizures in the past (Table 4). Their alcohol levels at admission were significantly higher than the levels in

Table 4. Admission Alcohol Levels in Clients With and Without a History of One or More Withdrawal Seizures

	Mid-Missouri Mental Health Center (MMMHC) n = 84*	Harry S Truman Memorial Veterans Hospital (HSTMVH) n = 98*
History of Withdrawal Seizures		
No	32 mmol/L (150 mg/dL) n = 67 SEM = 3	26 mmol/L (120 mg/dL) n = 85 SEM = 3
Yes	58 mmol/L (270 mg/dL) n = 17 SEM = 8	54 mmol/L (250 mg/dL) n = 13 SEM = 9
	P < .001†	P = .005†

*Number of patients does not equal total number who had an alcohol level determined because of missing data.

†By t tests.

those without such a history (by t tests, $P = .005$ for the HSTMVH patients, $P < .001$ for the MMMHC clients). In both institutions, those with a history of withdrawal seizures tended to present for care sooner after they had stopped drinking, 8 vs 36 hours at HSTMVH ($P < .001$ by t test) and 4 vs 13 hours at MMMHC ($P = .1$, with data recorded in only 28 cases). When those with a history of withdrawal seizures were compared with those without, there were no significant differences in estimates of the amount of alcohol consumed ($P = .8$ in the HSTMVH data, $.4$ in the MMMHC data, by t tests).

An estimate of the number of hours since the patient had his or her last drink was not significantly correlated with the severity of withdrawal in the analysis of data from either institution, either on univariate or multivariate analysis. The inclusion of the number of hours since the last drink as an independent variable in the regression models did not affect the association of admission alcohol level with the severity of withdrawal. Adjusting the alcohol level at admission for the time elapsed since the last drink (by adding 5.8 mmol/L [27 mg/dL] for each hour, based on the findings of Clothier et al⁴) did not change the correlation of alcohol level with severity of withdrawal.

Discussion

The results indicate that a patient's alcohol level at the time of admission is correlated with the severity of withdrawal in all of the three ways examined: the withdrawal severity assessment scores (at MMMHC), the amount of chlordiazepoxide used over the first 48 hours (at HSTMVH), and the severity of tremor with or without medical treatment of withdrawal (at both institutions). Though its predictive power may be limited, the alcohol level at admission appears to contribute more to our ability to predict the course of withdrawal than any other variable examined.

Although Clothier et al⁴ concluded that the alcohol level at admission was of no value clinically, our analysis of the raw data in their paper showed a correlation coefficient of .58 ($R^2 = .34$, $P = .02$). A measure of effect size (the slope of the regression line) was almost identical to that in the HSTMVH data in this study, lending further credibility to the association found.

Liver enzyme levels, which also correlated with measures of withdrawal severity in our study, are not as readily available in many situations as breath alcohol levels. Liver enzyme levels did not correlate with the severity of withdrawal as highly as alcohol levels did in this study, and complemented alcohol levels as a predictor of outcome.

Amount of alcohol consumed per day, as reported by the patients, did not predict the severity of withdrawal in either institution. This is in contrast to the findings of Pristach et al.³ These authors carefully obtained a history of recent alcohol consumption, and that attention to detail may have made possible a more accurate prediction of outcome. They also focused on consumption during the previous 7 days only, raising the possibility that *recent* consumption may have more of an effect on withdrawal severity than an individual's *usual* intake does. However, fewer than half of their patients had detectable alcohol levels at admission, suggesting a need for further study before their findings can be generalized to other patient groups.

Duration of drinking problems was shown to have no correlation with withdrawal severity in the study by Pristach et al.³ and a paradoxically negative correlation in the study by Shaw et al.² In our study, no meaningful association was found between withdrawal severity and either the number of years of drinking problems or the number of months of continuous daily drinking.

Clients at MMMHC who needed to be transferred for medical detoxification had higher alcohol levels at admission. This finding suggests that the alcohol level might allow staff in nondrug detoxification units to identify earlier those clients who may need to be transferred to a medical detoxification unit. A threshold of 33 mmol/L (150 mg/dL) may be of some value in identifying those persons who may need further care. At MMMHC, of those with a level of 33 mmol/L (150 mg/dL) or less, none required transfer for medical detoxification, and only one of 42 clients had any withdrawal assessment score high enough to prompt medical consultation. The negative predictive value of this cutoff may prove particularly useful in nondrug, social detoxification settings.

The lack of demonstrated reliability and validity of the withdrawal severity assessment score used at MMMHC is a major weakness in this study. The staff at MMMHC have found the scale to be clinically trustworthy, however, and similar associations were found with other outcome variables in this study. Using the area under the withdrawal-assessment-score curve seems more appropriate to us than using the maximum withdrawal score, and these two variables (area under the curve and maximum score) are highly correlated ($r = .83$). Whether the area under the curve is a better outcome measure, however, is open to debate and further testing.

Approximately half of the clients at MMMHC are admitted involuntarily. Patients admitted involuntarily may have higher alcohol levels and a more complicated course; confounding may cause the apparent relationship between the alcohol level at admission and the course and

outcome of detoxification. Unfortunately, we did not examine this variable, and further study will be needed. All patients at HSTMVH, however, enter voluntarily; therefore, confounding does not explain all of the relationships found.

The association between alcohol level at admission and the client's decision to remain on either unit for alcoholism rehabilitation suggests areas for further study. Those who were less intoxicated at the time of admission may have been more active in their decision to enter therapy, aware that detoxification is just the first step. Also, those who had higher alcohol levels may have had greater tolerance, slower metabolism, or some other biochemical factor that affected their willingness to enter rehabilitation. Whatever the explanation, higher alcohol levels are significantly correlated with a decreased likelihood of an individual's remaining on a treatment unit for rehabilitation following detoxification. This finding may help identify those who might benefit from more intensive efforts during detoxification to engage them in subsequent rehabilitation.

The finding of higher mean alcohol levels at admission among those with a history of one or more withdrawal seizures is intriguing and needs further exploration. Do they have higher alcohol levels because they enter treatment earlier in the course of withdrawal, wanting to avoid another seizure? Or do they have higher levels *and* a greater likelihood of withdrawal seizures because they drink more heavily or differ in other ways?

These results suggest that alcohol levels at admission to a treatment unit may help identify those persons at greater risk of more severe withdrawal and those less likely to remain for rehabilitation following detoxification. In addition, this study suggests further areas of research, both in the alcohol withdrawal syndrome and in biochemical and psychosocial factors related to an individual's decision to enter alcoholism treatment.

Acknowledgment

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