Individualized Treatment for Outpatients Withdrawing From Alcohol

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Background: This prospective study addressed the applicability of symptom-triggered detoxification to the outpatient setting.

Method: We studied 108 alcohol-dependent patients consecutively enrolled in an outpatient detoxification program between January 17, 1995, and October 17, 1995. The diagnosis was confirmed by verifying, through chart review, that patients met DSM-IV criteria for alcohol dependence. Patients were prescribed chlordiazepoxide according to a symptom-triggered detoxification protocol that utilized a standardized withdrawal scale. We compiled outcome data by reviewing the chart and the computerized medical record. Outcome was operationally defined to include completion of outpatient detoxification as well as outcome measures that were used in earlier studies of symptom-triggered detoxification in the hospital setting.

Results: Chlordiazepoxide was administered to only 41 patients (38%), yet 92 (85%) of the 108 enrolled successfully completed outpatient detoxification without medical complications. The patients who took chlordiazepoxide received a mean ± SD total of 167.2 ± 123.5 mg administered over 2.7 ± 1.4 days. Mean γ-glutamyltransferase levels were higher for the group of patients who subsequently received chlordiazepoxide (132.8 ± 312.1 IU/L compared with 56 ± 80.3 IU/L; Wilcoxon rank sum test, $t = 2600.5$, $p < .01$).

Conclusion: This study is the first to support the feasibility of symptom-triggered detoxification from alcohol in an outpatient setting. Our completion rate compared favorably with completion rates from previous studies of outpatient detoxification from alcohol using fixed-dose schedules. The percentage of patients receiving chlordiazepoxide and mean total amount of chlordiazepoxide administered in our study were also comparable to results from previous studies of symptom-triggered detoxification with hospitalized patients.

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Individualized treatment for alcohol withdrawal symptoms may have been conceptualized when Victor[1] recommended that the need for medication be determined by an estimation of the patient's status. Currently used terms for this technique are *symptom-triggered detoxification* or *symptom-triggered sedation*.[2,3] Symptom-triggered detoxification has usually incorporated a standardized withdrawal scale to determine benzodiazepine requirements during alcohol withdrawal.[2–6]

There have been no previous studies of the applicability of symptom-triggered detoxification to the outpatient setting. All of the prior research focused on hospitalized patients.[2–7] Symptom-triggered protocols have differed regarding the particular withdrawal scale, the frequency of withdrawal assessment, the cutoff scores for administration of sedative-hypnotic medication, the specific medication, and the appropriate dosage of medication.[2–7]

The preferred detoxification protocol in outpatient settings has been fixed-schedule therapy, during which a standard course of benzodiazepine was administered then gradually tapered and discontinued.[8–12] Fixed-schedule protocols have differed regarding which benzodiazepine was administered, the amount administered, and the rapidity of the taper.[8–12]

A few investigators have suggested that outpatients in mild to moderate alcohol withdrawal can be treated without sedative-hypnotic medication.[13–15] However, nonpharmacologic treatment for alcohol withdrawal may result in considerable morbidity and may be an ineffective utilization of resources.[13]

Matching patient symptomatology with appropriate sedative-hypnotic therapy can prevent both overtreatment and undertreatment for alcohol withdrawal.[2] Saitz et al.[3] suggested that future studies should identify patient populations for whom symptom-triggered therapy may be appropriate. Therefore, we chose to study the feasibility of symptom-triggered detoxification in an outpatient detoxification program.

METHOD

Subjects

We studied 108 alcohol-dependent patients consecutively enrolled in an outpatient detoxification program be-

tween January 17, 1995, and October 17, 1995. Enrolled patients reported recent heavy alcohol use; had a Modified Selective Severity Assessment (MSSA) score for alcohol withdrawal of 18 or less[6]; had no history of delirium tremens or seizures and no comorbid problem requiring an inpatient level of care; and had a negative breath or blood alcohol level. They did not report current substance use other than alcohol and tobacco products.

We confirmed the diagnosis of alcohol dependence through chart review, verifying that patients met DSM-IV[16] criteria. Data from the chart were also used to determine each patient's level of drinking, based on a composite measure reflecting the average daily ethanol consumption from all alcoholic beverages. The levels corresponded to National Institute of Alcohol Abuse and Alcoholism guidelines for categorizing light, moderate, and heavy drinkers.[17]

Outpatient Detoxification

Patients received vitamin supplements and submitted a breath analysis for alcohol each day. Vital signs were collected twice a day for 3 days and then daily.

Since long-acting benzodiazepines have been safely prescribed in outpatient settings,[9,10] chlordiazepoxide hydrochloride was used for our program. We did not select shorter-acting benzodiazepines because these might have allowed breakthrough withdrawal symptoms. The flexibility of our protocol allowed dosage adjustments for older and more debilitated patients.

Program staff assisted patients in reading a consent form for the use of chlordiazepoxide. After signing the consent form, patients were prescribed chlordiazepoxide according to the following protocol.

We selected the MSSA[6] (Table 1) because, unlike other withdrawal scales,[3,4] the MSSA did not require modification to include the patient's heart rate. Tachycardia has been used as a determinant factor in administering medication.[7] Since a patient with tachycardia will score at least 4 on the MSSA, we adopted a cutoff score of 4 or higher for administration of chlordiazepoxide. Because of the outpatient setting, assessment of withdrawal was limited to once a day in comparison to every 1 to 8 hours in inpatient settings.[2–6] Therefore, we implemented a relatively low threshold for medication administration to prevent progression of withdrawal between assessments.

Patients with MSSA scores of 3 or lower could receive chlordiazepoxide at their physician's discretion. Patients with MSSA scores of 4 or higher would receive chlordiazepoxide unless the treating physician documented that the elevated MSSA score did not result from withdrawal. We differentiated between patients exhibiting milder or more severe withdrawal, as recommended in a prior study[10]: patients with MSSA scores between 4 and 12 received as much as 100 mg/day of chlordiazepoxide, and those with scores between 13 and 18 received up to 200 mg/day of chlordiazepoxide. Our protocol's maximum daily dosages

Table 1. Items From the Modified Selective Severity Assessment (MSSA)*

1. Eating	3 to 4 = Ate about half of prior meal 7 = Ate none at all
2. Tremor	1 = Tremor not visible but can be felt 7 = Marked tremor even when arms are not extended
3. Sleep	1 = Patient gets up once 7 = Completely sleepless
4. Sensorium	1 = Knows correct date but is uncertain 3 = Disoriented for time by more than 2 days
5. Hallucinations	1 = Auditory hallucinations 4 = Fused auditory and visual hallucinations
6. Contact	1 = Drifts off slightly 7 = Makes no contact with examiner
7. Agitation	1 = Somewhat more than normal activity 7 = Paces back and forth
8. Sweating	1 = Barely perceptible sweating 7 = Drenching sweats
9. Temperature	1 = 99.5°F or below 9 = 103°F and over
10. Pulse	1 = 70 to 79 beats per minute 9 = 150 beats per minute and over

*The MSSA is a document in the public domain. Scores of 0 are possible on all items except temperature. Mid-range scoring criteria for each item are available from the authors on request, but are not included in this table because of space limitations.

fell within the range administered in previous studies.[2,7] Other than recommending a daily maximum, dosages for particular MSSA scores were not specified.

When patients no longer required chlordiazepoxide and had achieved at least 3 consecutive MSSA scores of 3 or lower, detoxification was ended. Clinicians separate from the detoxification staff confirmed that the patients were ready for placement in alcohol rehabilitation programs.

Statistical Analyses

We compared γ-glutamyltransferase (GGT) and aspartate aminotransferase (AST) levels for patients who received chlordiazepoxide versus those who did not by using the Wilcoxon rank sum test. We compared the number of abnormally high GGT and abnormally high AST levels between patients who did and did not receive chlordiazepoxide by chi-square analysis. In addition, we used a Spearman rank correlation to determine whether a correlation existed between maximum MSSA scores for patients who received chlordiazepoxide and the total amount of chlordiazepoxide received.

Outcome Measures

We compiled data by means of chart reviews. Since charts were inaccessible for a few patients, we also accessed data through the computerized tracking of prescription profiles, laboratory test results, and routine clerical processes. Data retrieval was accomplished objectively by individuals who did not play a major clinical role with these patients.

To verify whether the clinicians used the MSSA to guide medication requirements, we correlated the maxi-

Table 2. Comparison of Outpatients According to Chlordiazepoxide Administration During Symptom-Triggered Detoxification*

	Chlordiazepoxide Administered (N = 41)		Chlordiazepoxide Not Administered (N = 67)	
Characteristic[a]	Value	Range	Value	Range
Maximum MSSA score	8.0 ± 4.0[b]	2–18	4.0 ± 1.9	1–12
Total chlordiazepoxide, mg	167.2 ± 123.5	25–600	0	n/a
Days chlordiazepoxide	2.7 ± 1.4	1–6	0	n/a
First day dosage, mg	72.8 ± 44.5	20–200	0	n/a
GGT,[c] IU/L	132.8 ± 312.1	8–1997	56.0 ± 80.3[b]	13–623[b]
AST, U/L	42.2 ± 37.2	14–202	35.2 ± 40.6[d]	14–272[d]
GGT > 65 IU/L, N (%)	17 (41%)	n/a	15 (23%)[b]	n/a
AST > 41 U/L,[e] N (%)	14 (34%)	n/a	8 (12%)[d]	n/a

*Abbreviations: GGT = γ-glutamyltransferase, AST = aspartate aminotransferase.
[a]Values are mean ± SD unless otherwise noted.
[b]Information unavailable for 2 patients.
[c]GGT levels significantly higher for patients receiving chlordiazepoxide per Wilcoxon rank sum test, $t = 2600.5$, $p < .01$.
[d]Information unavailable for 1 patient.
[e]Significantly more abnormally high AST levels for patients receiving chlordiazepoxide, $\chi^2 = 6.22$, $df = 1$, $p < .02$.

mum MSSA scores for patients who received chlordiazepoxide with the total amount received during their detoxification. We also correlated the age of the patients who received chlordiazepoxide with the total amount received. This correlation assisted in confirming whether our protocol allowed dosage reductions for older patients. To gauge whether the cutoff score was utilized, we determined the number of patients who had scores of 4 or higher on the MSSA but did not receive chlordiazepoxide.

Outcome was operationally defined to include measures from studies of outpatient detoxification: completion,[8–12,18] dropping out,[9,12,19] or discharge. We also incorporated outcome measures from studies of symptom-triggered detoxification: the percentage of patients receiving sedative-hypnotic medication,[3,4,6,7] the mean total dose administered,[2–4,7] the number of days patients received sedative-hypnotic medication,[3,5,7] and the relationship between the degree of alcohol exposure (as determined by liver function tests) and benzodiazepine administration.[5] The liver function tests we selected were GGT and AST, since these have been used as markers of heavy drinking.[20]

RESULTS

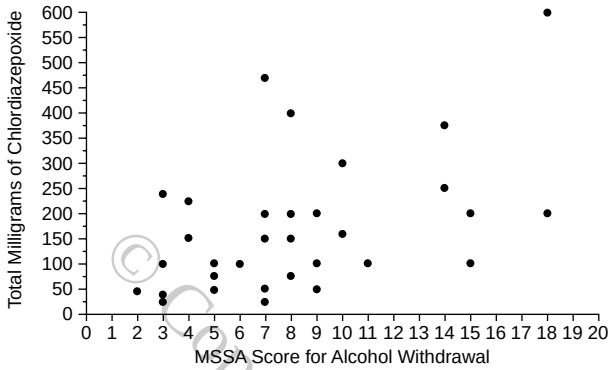
Most of the 108 outpatients in the sample were men (N = 107, 99%), not currently married (N = 73, 68%), who had a high school education (mean ± SD years = 12.3 ± 2.4). Their mean age was 47.2 ± 8.4 years, and they reported having a problem with alcohol for a mean ± SD duration of 17.0 ± 11.0 years. Eighty-eight patients (81%) were white, and the other 20 patients (19%) were black. Of the 102 patients for whom employment and income data were available, 82 patients (80%) were unemployed at the time of the study, and 72 patients (71%) earned less than $10,000 during the past year. At least 61 patients (56%) had been previously treated for alcohol problems. All 101 patients for whom data were available met criteria for classification as heavy drinkers. Although the patients averaged 5.6 ± 4.0 days since their last drink, over half (52/102) reported 4 or fewer days.

The patients averaged 4.6 ± 2.0 days of outpatient detoxification enrollment, and most of them (N = 97, 90%) utilized Veterans Affairs–supported housing. Chlordiazepoxide was administered to only 41 patients (38%), yet 92 (85%) of the 108 enrolled successfully completed outpatient detoxification without medical complications. Of the 16 patients who did not complete outpatient detoxification, 11 were removed from the program and 5 dropped out of the program. Over half (21/41) of the patients who received chlordiazepoxide reported 3 or fewer days since their last drink; thus, chlordiazepoxide was administered frequently to patients in early stages of withdrawal. However, some patients received chlordiazepoxide as long as 14 days after their last drink.

In Table 2, patients are compared according to chlordiazepoxide administration. The 41 patients who received chlordiazepoxide averaged a total of 167.2 ± 123.5 mg administered over 2.7 ± 1.4 days. Mean GGT levels were significantly higher for the group of patients who subsequently received chlordiazepoxide (Wilcoxon rank sum test, $t = 2600.5$, $p < .01$). There was insufficient power to detect a significant difference in the average AST levels for the 2 groups, but patients who subsequently received chlordiazepoxide were significantly more likely to have had an abnormally high AST level ($\chi^2 = 6.22$, $df = 1$, $p < .02$).

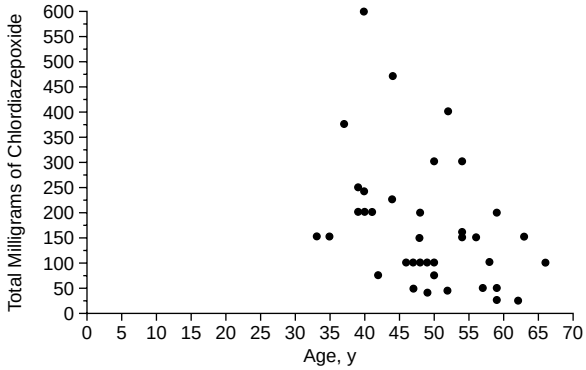
A Spearman rank correlation between the maximum MSSA scores for patients who received chlordiazepoxide and the total amount received was significant ($\rho = 0.48$, $p < .003$): patients with higher MSSA scores received more chlordiazepoxide (Figure 1). There was also a sig-

Figure 1. Relationship Between MSSA Score and Total Chlordiazepoxide Administered (N = 39 Patients)*



*MSSA score not available for 2 patients who received chlordiazepoxide. Five pairs and 1 group of 3 patients had identical MSSA/dose combinations.

Figure 2. Relationship Between Patient Age and Total Chlordiazepoxide Administered (N = 41 Patients)*



*Two pairs and 1 group of 3 patients had identical age/dose combinations.

nificant Spearman rank correlation between the age of the patients who received chlordiazepoxide and the total amount received ($\rho = -0.44$, $p < .005$): older patients received less chlordiazepoxide (Figure 2).

Thirty-three patients who had scores of 4 or higher on the MSSA did not receive chlordiazepoxide; however, 18 of these patients had a maximum score of only 4. The clinicians' explanations for not administering chlordiazepoxide to patients with elevated scores included the following: essential tremor; tachycardia due to dental extraction or recent heavy cigarette use; chronic insomnia; and insomnia due to antidepressant withdrawal, nocturia, or posttraumatic stress disorder.

DISCUSSION

This was the first documented study of the applicability of symptom-triggered detoxification to the outpatient setting. The 85% completion rate compared favorably with previously reported rates from other outpatient detoxification programs.[8–13,18,19] The percentage of patients who received chlordiazepoxide and the mean total amount of the drug received fell within the ranges reported in studies of symptom-triggered detoxification with hospitalized patients.[2–7] Sullivan et al.[5] speculated that patients who were not given medication might think that they were being denied treatment. However, this speculation seems unfounded, since 85% of our patients completed detoxification even though only 38% received medication.

Correlational results from our study confirmed that the clinicians used the withdrawal scale to guide medication requirements and that the flexibility of the protocol allowed dosage reductions for older patients. Sullivan et al.[5] suggested that older patients may be overmedicated by fixed-dose regimens. Future research might clarify whether symptom-triggered detoxification is the most appropriate protocol for older patients, since individualizing pharmacotherapy has been identified as important for these patients.[21] Our protocol enabled the clinicians to limit the chlordiazepoxide dosage to the smallest effective amount in older patients, as recommended by the *Physicians' Desk Reference*.[22]

Support for the value of our protocol was demonstrated by the significant relationships between the degree of alcohol exposure (as determined by liver function tests) and benzodiazepine administration. Patients with higher average results or abnormal results on their liver function tests were more likely to have subsequently received chlordiazepoxide. The liver function tests were obtained at clinic enrollment, and the results were usually not available to the clinicians until after medication decisions were made. In addition, chlordiazepoxide administration occurred after laboratory examinations were done, so the medication did not cause the elevations.

These findings have limited applicability to similar samples of patients. Our sample consisted largely of white and black men who were categorized as heavy drinkers and as having lower income. Most patients were in early stages of withdrawal at clinic enrollment. Although symptoms of alcohol withdrawal typically begin within the first day of abstinence and peak in intensity during the second day,[23] not all patients fit the typical profile.[24] Our protocol accommodated these "atypical" patients.

Such patients may have received no treatment in a fixed-schedule protocol, especially if the protocol was restricted to patients in early withdrawal. However, a randomized study comparing fixed-schedule to symptom-triggered detoxification in outpatients matched for time since last drink would provide a more definitive contrast of these techniques.

Another limitation of our study was the flexibility of the protocol. The physician could elect not to administer chlordiazepoxide to patients whose withdrawal scale

scores met or exceeded the cutoff, if the elevated scores did not result from withdrawal. Future research comparing higher to lower cutoff scores and flexible to rigid symptom-triggered protocols is needed.

There may be advantages to maintaining a more flexible protocol. Sullivan et al.[5] speculated that if a withdrawal scale is regularly administered, patients may learn which responses result in medication administration, setting up drug-seeking behavior. However, this possibility might be less likely if the physician could withhold medication when elevated scores were unrelated to withdrawal.

Medication doses in symptom-triggered detoxification are based on the patient rather than on some arbitrary fixed schedule learned in medical school or residency training. Liability for the physician may be reduced using this technique, since patients do not routinely receive sedative-hypnotic medication. Other methods to reduce liability, improve safety, and enhance compliance in the outpatient setting include daily standardized assessment and documentation of withdrawal, prescription of the smallest amount of medication necessary to last until the next appointment, consent forms advising patients not to drive or operate machinery, housing and transportation support for homeless patients, and treatment contracts specifying program rules and regulations.

Our study represents an incremental advance in alcohol detoxification treatment by employing a symptom-triggered protocol in the outpatient setting. In an era of managed care and very finite resources, this could become a valuable approach.

Drug name: chlordiazepoxide (Librium and others).

REFERENCES

1. Victor M. Treatment of alcoholic intoxication and the withdrawal syndrome. Psychosom Med 1966;28:636–650
2. Wartenberg AA, Nirenberg TD, Liepman MR, et al. Detoxification of alcoholics: improving care by symptom-triggered sedation. Alcohol Clin Exp Res 1990;14:71–75
3. Saitz R, Mayo-Smith MF, Roberts MS, et al. Individualized treatment for alcohol withdrawal. JAMA 1994;272:519–523
4. Foy A, March S, Drinkwater V. Use of an objective clinical scale in the assessment and management of alcohol withdrawal in a large general hospital. Alcohol Clin Exp Res 1988;12:360–364
5. Sullivan JT, Swift RM, Lewis DC. Benzodiazepine requirements during alcohol withdrawal syndrome: clinical implications of using a standardized withdrawal scale. J Clin Psychopharmacol 1991;11:291–295
6. Benzer DG. Quantification of the alcohol withdrawal syndrome in 487 alcoholic patients. J Subst Abuse Treat 1990;7:117–123
7. Worner TM. Propranolol versus diazepam in the management of the alcohol withdrawal syndrome: double-blind controlled trial. Am J Drug Alcohol Abuse 1994;20:115–124
8. Hayashida M, Alterman AI, McLellan AT, et al. Comparative effectiveness and costs of inpatient and outpatient detoxification of patients with mild-to-moderate alcohol withdrawal syndrome. N Engl J Med 1989;320:358–365
9. Stinnett JL. Outpatient detoxification of the alcoholic. Int J Addict 1982;17:1031–1046
10. Collins MN, Burns T, Van Den Berk AH, et al. A structured programme for out-patient alcohol detoxification. Br J Psychiatry 1990;156:871–874
11. Alterman AI, Hayashida M, O'Brien CP. Treatment response and safety of ambulatory medical detoxification. J Stud Alcohol 1988;49:160–166
12. Webb M, Unwin A. The outcome of outpatient withdrawal from alcohol. Br J Addict 1988;83:929–934
13. Whitfield CL, Thompson G, Lamb A, et al. Detoxification of 1,024 alcoholic patients without psychoactive drugs. JAMA 1978;239:1409–1410
14. Naranjo CA, Sellers EM, Chater K, et al. Nonpharmacologic intervention in acute alcohol withdrawal. Clin Pharmacol Ther 1983;34:214–219
15. Castaneda R, Lifshutz H, Galanter M. Treatment compliance after detoxification among highly disadvantaged alcoholics. Am J Drug Alcohol Abuse 1992;18:223–234
16. American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition. Washington, DC: American Psychiatric Association; 1994
17. Richards MS, Goldberg J, Rodin MB, et al. Alcohol consumption and problem drinking in white male veterans and nonveterans. Am J Public Health 1989;79:1011–1015
18. Feldman DJ, Pattison EM, Sobell LC, et al. Outpatient alcohol detoxification: initial findings on 564 patients. Am J Psychiatry 1975;132:407–412
19. O'Connor PG, Gottlieb LD, Kraus ML, et al. Social and clinical features as predictors of outcome in outpatient alcohol withdrawal. J Gen Intern Med 1991;6:312–316
20. Irwin M, Baird S, Smith TL, et al. Use of laboratory tests to monitor heavy drinking by alcoholic men discharged from a treatment program. Am J Psychiatry 1988;145:595–599
21. Shader RI, Kennedy JS. Psychopharmacology. In: Kaplan HI, Sadock BJ, eds. Comprehensive Textbook of Psychiatry, vol 2. 6th ed. Baltimore, Md: Williams & Wilkins; 1995:2603–2615
22. Librium (chlordiazepoxide hydrochloride). Physicians' Desk Reference. Montvale, NJ: Medical Economics; 1997:2331–2332
23. American Psychiatric Association. Practice guideline for the treatment of patients with substance use disorders: alcohol, cocaine, opioids. Am J Psychiatry 1995;152(11, suppl):7–8
24. Winger G, Hofmann FG, Woods JH. Depressants of the CNS: alcohol, barbiturates, and benzodiazepines. In: A Handbook on Drug and Alcohol Abuse: The Biomedical Aspects. 3rd ed. New York, NY: Oxford University Press; 1992:57–73