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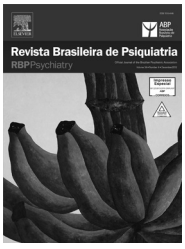

ORIGINAL ARTICLE

Psychosocial and clinical predictors of retention in outpatient alcoholism treatment

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Abstract
Objective: One of the factors associated with low rates of compliance in the treatment for alcoholism seems to be the intensity of craving for alcohol. This study aimed to evaluate the associations between alcohol craving and biopsychosocial addiction model-related variables and to verify whether these variables could predict treatment retention. *Methods*: The sample consisted of 257 male alcoholics who were enrolled in two different pharmacological trials conducted at the Universidade de São Paulo in Brazil. Based on four factors measured at baseline – biological (age, race, and family alcoholism), psychiatric (depression symptoms), social (financial and marital status), and addiction (craving intensity, severity of alcohol dependence, smoking status, drinking history, preferential beverage, daily intake of alcohol before treatment) – direct logistic regression was performed to analyze these factors' influence on treatment retention after controlling for medication groups and AA attendance. *Results*: Increasing age, participation in Alcoholics Anonymous groups, and beer preference among drinkers were independently associated with higher treatment retention. Conversely, higher scores for depression increased dropout rates. *Conclusion*: Health services should identify the treatment practices and therapists that improve retention. Information about patients' characteristics linked to dropouts should be studied to render treatment programs more responsive and attractive, combining pharmacological agents with more intensive and diversified psychosocial interventions.

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Preditores psicossociais e clínicos de retenção ao tratamento para alcoolismo

Resumo
Objetivo: Um dos fatores associados com baixas taxas de adesão ao tratamento para alcoolismo parece ser a intensidade da fissura pelo álcool. Este estudo objetiva avaliar a associação entre a fissura pelo álcool e variáveis relacionadas ao modelo biopsicossocial de dependência, bem como verificar se estas variáveis prevêem retenção ao tratamento. *Método*: A amostra foi composta por 257 homens dependentes de álcool que participaram de dois diferentes estudos clínicos que foram desenvolvidos na Universidade de São Paulo, Brasil. Baseado em quatro fatores medidos no início do tratamento – biológico (idade, raça e alcoolismo familiar), psiquiátrico (sintomas depressivos), social (condição econômica e status marital) e relacionado à dependência (intensidade da fissura, gravidade da dependência do álcool, status de ser fumante, tempo de consumo regular e problemático de bebidas alcoólicas, bebida preferencial, quantidade de etanol consumido ao dia) – um modelo de regressão logística direta foi desenvolvido para analisar o efeito destas variáveis sobre a retenção ao tratamento, controlando para a influência das medicações utilizadas e da participação em grupos de alcoólicos anônimos. *Resultados*: Mais idade, participação em grupos de alcoólicos anônimos e preferência por cerveja foram fatores independentemente associados a maior retenção ao tratamento. Maior escore em depressão aumentou a chance de abandono. *Conclusão*: Serviços de saúde devem identificar práticas e profissionais que proporcionem melhora nas taxas de retenção. Informação sobre as características dos pacientes relacionadas ao abandono devem ser usadas para tornar programas de tratamento mais eficientes e atraentes, combinando agentes farmacológicos com mais intensivas e diversificadas intervenções psicossociais.

Introduction

The rates of compliance with treatment for alcoholism are as low as those for other chronic medical disorders. Poor treatment adherence represents a reduction in quality of life and a loss of life years for many patients. Over the last 30 years, researchers have identified several client-centered factors associated with early discontinuation of substance abuse treatment, such as youth, single social status, high severity of substance use, family alcoholism, and depression. With regard to treatment-centered factors, negative therapeutic alliance, low clinician experience, and inadequate engagement of family members in treatment have been associated with high rates of treatment abandonment and relapses during follow-up.[1,2]

Many of these client-centered factors have been positively correlated with craving intensity. Despite the subjective nature of and diverse theories surrounding this theme, craving has been positively correlated with younger age,[3] alcohol dependence severity,[4] family alcoholism,[5] and negative moods or emotional status.[6] Other factors, such as stress exposure,[7] preferred beverage,[8] history of recurrent detoxifications,[9] and smoking status,[10] have also been associated with craving intensity. Hence, craving has been considered a better predictor of relapse than other variables, such as psychosocial functioning, treatment duration, and alcoholism severity levels.[5]

Alcohol craving is thought to appear either from the desire to have alcohol's positive effects (i.e., positive reinforcement) or from the desire to circumvent the negative effects of withdrawal symptoms (i.e., negative reinforcement), but further models have proposed other important dimensions of craving, such as the desire and intention to consume alcohol, lack of control over alcohol use, preoccupation with drinking-related thoughts and/or behavior among others. Therefore, certain aspects of craving can better characterize the experience of some alcoholics than that of others, which can render the evaluation of craving extremely difficult.[11] In addition, the quality and intensity of craving can vary in accordance with personal characteristics and environmental circumstances.

Treatments for alcoholism have been developed to reduce craving and, consequently, alcohol consumption. Currently, four agents are approved by the Food and Drug Administration to treat alcoholism: disulfiram, acamprosate, oral naltrexone, and once-monthly, injectable, extended-release naltrexone. Notwithstanding some inconsistent findings, these agents have demonstrated some ability to reduce craving and increase abstinence time. Except for disulfiram, which has an aversive mechanism of action, effective pharmacotherapies for alcohol dependence are thought to work by blocking the rewards of alcohol or by stabilizing the systems dysregulated by chronic alcohol intake, making craving less intense.[12] In addition, off-label medications, such as topiramate and ondansetron, have also been shown to reduce craving and increase abstinence time.[13,14] The ability to reduce craving should then be associated with the likeliness to increase treatment retention, at least to some extent.

A range of studies have demonstrated that longer durations of treatment and treatment completion are associated with better outcomes in alcoholism-treatment programs.[15] We are aware that treatment retention is not an outcome measurement on its own; however, the capacity to retain patients in active participation is a sensible measurement associated with the quality and efficacy of health care.

Additionally, according to the UK's National Treatment Agency for Substance Misuse, retention in drug treatment is the best available measurement of treatment effectiveness.[16]

In this present study, we evaluated the associations between alcohol craving (measured using the Obsessive Compulsive Drinking Scale – OCDS) and diverse previously tested variables in the biopsychosocial addiction model. Specifically, we investigated the relationship of alcohol craving with the following factors: (1) biological: age, race, and family alcoholism; (2) addiction: severity of alcohol dependence, smoking status, drinking history, preferred beverage, and daily intake of alcohol before treatment; (3) psychiatric: depression symptoms; and (4) social: financial and marital status. Additionally, we evaluated whether craving intensity and any of the above variables could predict treatment retention, when different pharmacotherapies and participation in Alcoholics Anonymous groups were also taken into account. In addition, given the role of craving intensity on attrition rates, we hypothesized that craving (measured by the OCDS) would be a strong predictive factor of treatment, even after controlling for other variables potentially correlated with this variable.

Methods

Databases of two randomized, double-blind, placebo-controlled clinical trials were combined for this joint analysis. These trials were performed to detect the efficacy of active medications in reducing drinking, promoting abstinence and decreasing cravings in alcohol-dependent outpatients. The pharmacological treatments lasted 12 weeks. Each study was approved by the Ethics Committee of the Clinical Hospital of the Universidade de São Paulo in Brazil. More specifically, we combined the databases from the following double-blind studies, which evaluated craving intensity by applying the Obsessive Compulsive Drinking Scale (OCDS): (A) a trial, performed between 2004 and 2007, comparing topiramate (up to 300 mg/day), naltrexone (50 mg/day) and placebo;[14] and (B) a study, conducted between 2008 and 2010, comparing ondansetron (16 mg/day) with placebo. These trials were coordinated by the same doctor and were developed in the same clinical setting, following the same behavioral approaches and double-blind principle.

Participants

Male patients, 18-60 years of age, with an International Classification of Diseases (ICD-10; World Health Organization, 1992) diagnosis of alcohol dependence and who were enrolled as outpatients in the Assistance Sector of the Interdisciplinary Group of Studies on Alcohol and Drugs at the Universidade de São Paulo (GREA) were assessed for each trial. This service (GREA) is dedicated to the treatment of men who abuse or are dependent on alcohol and/or any other type of drug.

The exclusion criteria were (a) younger than 18 years of age or older than 60 years of age; (b) a current diagnosis of dependence or abuse of other substances except for nicotine; (c) patients with serious coexisting clinical diseases (e.g., inadequately controlled diabetes, cardiac failure, alcoholic cirrhosis); (d) previous treatment with any medication to treat alcoholism within six months of randomization; (e) concomitant psychiatric disorders that might require specific drug treatment; (f) inability to provide full informed consent; and (g) a clinical history of mental retardation, as it reduced the accuracy of the information given.

For each study, all of the subjects provided written informed consent. They were informed about the objectives of each study, the nature of the treatment offered, and the profiles of the medications tested and that the medications they would receive would be chosen at random. All of the patients were assured about the confidentiality of the data and were informed that they were free to withdraw their consent and discontinue participation in the studies at any time without prejudice regarding their continued medical care. All of the participants were encouraged to participate in Alcoholics Anonymous groups (AA), but this participation was not an obligatory condition of participating in these trials.

Measurements

In the first interview for each trial, after a full history and clinical examination, patients who fulfilled the inclusion criteria were evaluated. Socio-demographic data and lifetime drinking history, such as family antecedents of alcohol problems, daily intake of alcohol in grams, drinking onset age, age at onset of regular alcohol consumption, and problem drinking onset age, were obtained in a standardized semi-structured interview commonly used in the therapeutic setting of the Interdisciplinary Group of Studies on Alcohol and Drugs of the Clinical Hospital of the Universidade de São Paulo in Brazil.

All of the patients were evaluated at the first interview with the Short Alcohol Dependence Data (SADD),[17] the Hamilton Depression Rating Scale (HDRS),[18] and the Obsessive-Compulsive Drinking Scale (OCDS).[19] Blood was taken for a routine full blood count and for liver function tests.

A weighting scale was adopted to evaluate family alcoholism. The following grade was used: 0.5 points for first-degree relatives and 0.25 points for second-degree relatives. A rigorous analysis of the incidence of alcohol dependence in first- and second-degree relatives was performed in line with another study.[20]

Additionally, the participants were questioned about their current average daily consumption of beer, spirits, and wine, with regard to the duration of use and the time of drinking (morning, afternoon, or night). Beer preference drinkers were then defined as those who drank more beer than spirits or wine and accordingly for spirits and wine preference drinkers. For a more precise classification, we defined a particular type of alcoholic beverage as "predominant" if the consumption of that type of beverage accounted for two-thirds or more of the total of ethanol consumed during the last year. This classification was used in a previous study.[4]

At each appointment, the participants were also asked about their participation in AA, and those subjected that attended AA at least once a week were considered to be adherent to this self-help group.

Procedure

All of the patients underwent a two-week detoxification period prior to initiating active medication or placebo. This detoxification period was conducted on an outpatient basis, and the patients were given medications, such as lorazepam

up to 6 mg/day and vitamin B1 300 mg/day, in cases of the manifesting of withdrawal symptoms. Laboratory exams, including liver function, were collected during this period. The patients manifested minimal to moderate withdrawal symptoms, which allowed them to be treated on an outpatient basis.

At each appointment, all of the patients received standardized and manual brief cognitive behavioral interventions. The overall goal of these interventions was to increase the subjects' ability to cope with high-risk situations that could precipitate relapses. The following topics were standardized and applied to each patient during treatment: management of negative mood, assertiveness, drink refusal skills, enhancement of social support networks and relapse prevention.

For each trial, all capsules were adequately manufactured to have identical appearances, thus avoiding any double-blind violation.

Treatment retention was one of the outcome measurements used in this joint study. We considered three reasons for dropping out of the trials: (a) "refuses to continue" (the patient affirmed that he wanted to stop that type of treatment and to try others, e.g., psychotherapy only); (b) "protocol violation" (the patient used other pharmacologic drugs during the studies); and (c) "lost to follow-up" (the patient gave up following the studies and did not manifest any desire to be treated differently). The patients who remained in treatment for all 12 weeks were considered completers. The patients who did not attend follow-ups were considered discontinuers.

Data analysis

The Kolmogorov-Smirnov test was used to evaluate whether the variables were normally distributed. The following variables had to be square-root transformed: OCDS and HDRS mean levels and the quantity of ethanol per day. Direct logistic regression analysis (Wald's method) was performed to investigate associations between treatment outcome (completers versus discontinuers) and the following predictive variables measured at baseline: age, race, marital status, depressive symptoms (measured by HDRS), financial condition, marital status, time period since the regular drinking onset age, time period since the problem drinking onset age, preferred beverage, daily intake of alcohol before treatment, medication groups, AA attendance, severity of alcohol dependence (measured by SADD), and craving for alcohol (measured by OCDS). Given that all of the predictors were entered into the equation simultaneously (as long as tolerance was not violated), a predictor that was highly correlated with the outcome by itself might have shown little predictive capability in the presence of other highly correlated predictors. Therefore, we also computed the correlation matrix of the variables included in logistic regression analysis. Pearson's r, Φ and point-biserial correlation coefficients were used to indicate the relationships between two continuous variables, two categorical variables, and between one continuous variable and one categorical variable, respectively. The data were analyzed using SPSS Statistics for Windows, version 18.0.

Results

Our sample was composed of 257 men, aged between 23 and 60 years of age (mean 43.76; SD 8.92). Approximately 56% were married, 56% were white, 53% had not reached high school, and 65% were Christian. One hundred seventy-six (69%) reported being smokers. Out of 257 participants, 136 (52.92%) completed the studies. The baseline characteristics of this study population are displayed in Table 1.

As shown in Table 2, direct logistic regression analysis (Wald's method) was performed on group status (completers and discontinuers) as an outcome and on the following predictors: medication groups and participation in AA as treatment-related variables; and OCDS, SADD, and HDRS mean scores, age at the beginning of current treatment, time since the beginning of regular alcohol use, time since the problem drinking onset age, family alcoholism, preferred beverage, tobacco consumption, quantity of ethanol per day (before the current treatment), history of previous treatment for alcoholism, race, marital status, and financial situation were treated as variables possibly related to craving intensity. We chose this method despite the fact that some predictors could be strongly associated with other ones and, as a result, some of them could mask the effect of others. In this analysis, "age at the beginning of the current treatment", "participation in AA", "HDRS mean levels", and "beer preference drinkers" predicted treatment outcome. The model was statistically reliable, ($x^2 = 44.48$, 21 df, $p < 0.01$). The variance in group membership accounted for was low, with Nagelkerke $R^2 = 0.21$. The overall prediction success was 65.8%. We checked the fit of our model using Hosmer and Lemeshow's test ($x^2 = 8.15$, 8 df, $p = 0.42$).

We also performed another direct logistic regression analysis involving only the variables that were significantly associated with treatment retention in the previous analysis. As shown in Table 3, 'age at the beginning of the current treatment', 'participation in AA', and 'HDRS mean levels' remained significantly associated with treatment retention. Conversely, 'beer preference' did not predict retention in this latter analysis. This model was statistically reliable, ($x^2 = 24.55$, 5 df, $p < 0.01$). The variance in group membership accounted for was marginal, with Nagelkerke $R^2 = 0.12$. The overall prediction success was 65.4%. The model fit was checked using Hosmer and Lemeshow's test ($x^2 = 8.89$, 8 df, $p = 0.35$).

Table 4 shows correlation analyses involving variables measured at baseline. Although correlations inferior to 0.50 should be considered non-significant, we decided to show all correlations with p-values of less than 0.05. As shown in Table 4, OCDS was negatively associated with age at the beginning of each trial and with the status of being married but was positively correlated with family alcoholism, severity of alcohol dependence, preferential consumption of spirits, and quantity of ethanol consumed before each trial.

Discussion

This study supports previous evidence that alcohol craving is positively correlated with family alcoholism, dependence severity, and quantity of ethanol consumed per day but negatively associated with the patient's age. In addition, alcohol craving was positively correlated with a preference

Table 1 Baseline characteristics

Characteristic	Patients (n = 257)
Age, mean (SD)	43.76 (8.92)
Race, n (%)	
White	144 (56.03)
Black	33 (12.84)
Mixed race	80 (31.13)
Marital status, n (%)	
Married	144 (56.03)
Single	41 (15.95)
Separated/Widower	72 (28.02)
Quantity of ethanol per day (in grams),a mean (SD)	297.77 (178.41)
History of having received previous treatment for alcoholism, n (%)	139 (54.09)
Monthly income (in R$, the Brazilian currency), mean (SD)	1,085.72 (1002.35)
Preferred beverage, n (%)	
Spirits	183 (71.20)
Beer	71 (27.63)
Wine	3 (1.17)
Medication groups, n (%)	
Placebo	106 (41.24)
Topiramate	52 (20.23)
Naltrexone	49 (19.07)
Ondansetron	50 (19.46)
Smoking, n (%)	177 (68.87)
OCDS, mean (SD)	47.99 (12.18)
SADD, mean (SD)	27.73 (8.28)
HDRS, mean (SD)	9.90 (6.38)
Time since the regular drinking onset age (in years)	17.98 (9.63)
Time since the problem drinking onset age (in years)	11.19 (9.12)
Plasma GGT, U/L; (reference range 8-61), mean (SD)	144.56 (254.71)
Plasma ALT, U/L; (reference range < 41), mean (SD)	38.04 (29.16)
Plasma AST, U/L; (reference range < 37), mean (SD)	42.04 (35.27)
Plasma MCV, f/L; (reference range 80-100), mean (SD)	94.77 (7.22)

[a] Indicates alcohol usage during the last three months preceding each study.
OCDS: Obsessive Compulsive Drinking Scale; SADD: Short Alcohol Dependence Data; HDRS: Hamilton Depression Rating Scale; GGT: gamma-glutamyl transferase; ALT: alanine aminotransferase; AST: aspartate aminotransferase; MCV: mean cellular volume.

for spirits. Increasing age, lower scores for depression, beer preference, and AA attendance predicted higher treatment retention. Contrary to our initial hypothesis, the variable 'craving' (measured by the OCDS at baseline) was not a strong predictive factor of treatment retention.

Other studies on patients with impulsive behaviors have already shown a decrease in impulsive and compulsive symptoms with increasing age, and this relationship also seems to be true among alcoholics.[3] In fact, a progressive reduction of daily alcohol intake,[21] a decrease in mesolimbic neurotransmission, and changes in the hypothalamic-pituitary-adrenal (HPA)[22] and hypothalamic-pituitary-thyroid[23] axes have been hypothesized to be possible causal mechanisms for craving reduction with increasing age. Parallel to these studies, there has been some evidence that older age can predict better compliance with alcoholism treatment.[24]

In our study, higher scores for depression predicted early discontinuation of treatment. Despite this finding, research has shown mixed results regarding the relationship between depression symptoms and treatment retention.[25] Nevertheless, it is important to note that depression was positively correlated with longer drinking careers and more frequent histories of being previously treated for alcoholism. In fact, negative experiences with previous alcoholism treatment could have a negative impact on the future client's readiness to accept help for alcohol problems. The awareness that a previous experience was negative can powerfully change behavior and clinical outcomes.[26] It is also important to stress that no participant was severely depressed or required specific treatment for depression in the present study, given that depression was an exclusion criterion for both trials.

Beer preference drinkers showed higher treatment retention than spirits and wine preference drinkers. This finding was already discussed in a previous study published by our group.[4] This finding was different from other studies that reported higher craving among beer preference drinkers, probably due to the greater volume intake of beer compared to other beverages.[27] However, the influence of different types of beverages on craving and adherence to treatment can

Table 2 Effects of clinical and psychosocial variables at baseline on treatment retention (direct logistic regression)

Variables	SE	Wald	df	p	OR	CI (95%)
Age	0.02	4.96	1	0.02*	1.05	1.01-1.09
Race						
White (reference)	0.45	0.11	1	0.74	1.16	0.48-2.81
Black	0.33	2.55	1	0.11	0.59	0.31-1.13
Mixed races						
Marital status						
Married (reference)						
Single	0.42	1.01	1	0.31	1.52	0.67-3.45
Separated/Widowed	0.34	0.89	1	0.34	0.73	0.37-1.41
Quantity of ethanol per day (in grams)	< 0.01	0.14	1	0.71	> 0.99	0.99-1.01
Previous treatments for alcoholism	0.29	0.13	1	0.72	1.11	0.63-1.95
Monthly income	< 0.01	3.62	1	0.06	> 0.99	0.99-1.01
Preferred beverage						
Spirits (reference)						
Beer	0.33	4.07	1	0.04*	1.95	1.02-3.75
Wine	1.32	0.72	1	0.39	3.07	0.23-41.04
Medication groups						
Placebo (reference)						
Ondansetron	0.40	2.85	1	0.09	1.96	0.90-4.30
Naltrexone	0.40	2.20	1	0.14	1.82	0.82-3.99
Topiramate	0.40	1.55	1	0.21	1.65	0.75-3.65
Smoking	0.32	0.30	1	0.58	1.19	0.64-2.23
OCDS	0.02	< 0.01	1	0.95	0.99	0.97-1.03
SADD	0.02	< 0.01	1	0.94	1.01	0.95-1.05
HDRS	0.02	5.56	1	0.02*	0.95	0.90-0.99
Years since the regular drinking onset age	0.03	1.27	1	0.26	1.03	0.98-1.08
Years since the problem drinking onset age	0.02	2.44	1	0.12	0.96	0.92-1.01
AA Attendance	0.48	5.70	1	0.02*	3.12	1.23-7.97

* p < .05; ** p < .01;
OCDS: Obsessive Compulsive Drinking Scale; SADD: Short Alcohol Dependence Data; HDRS: Hamilton Depression Rating Sacle; AA: Alcoholics Anonymous.

Table 3 Direct logistic regression model including only the variables that were significantly associated with treatment retention in Table 2

Variables	*SE*	Wald	df	p	OR	CI (95%)
Age	0.02	9.16	1	< 0.01**	1.05	1.02-1.08
Preferred beverage						
Spirits (reference)						
Beer	0.30	3.52	1	0.06	1.75	0.98-3.15
Wine	1.26	0.17	1	0.68	1.68	0.14-19.89
HDRS	0.02	4.34	1	0.03*	0.96	0.92-0.99
AA Attendance	0.45	5.03	1	0.02*	2.73	1.13-6.55

* p < 0.05; ** p < 0.01;
HDRS, Hamilton Depression Rating Sacle; AA: Alcoholics Anonymous.

be a byproduct of several confounding variables, such as cultural and socioeconomic factors. Although greater volume intake among beer drinkers is related to craving intensity, mainly due to its influence on volume-regulating peptides, spirits drinkers can consume greater quantities of ethanol per day than beer drinkers. Alcohol craving is also associated with the daily amount of ethanol consumed and with the severity of alcohol dependence.[4] In our study, the correlations between these two variables (alcoholism severity and quantity of ethanol) in spirits drinkers were positive and significant.

Participation in AA was significantly correlated with retention in treatment. To date, there has been no conclusive scientific evidence that participation in AA keeps patients in treatment longer.[28] In general, one of the difficulties in evaluating the effectiveness of participation in AA is the self-selection bias of those who participate.[29] Because individuals self-select themselves for participation in AA, otherwise known as selection bias, it is not clear whether there are personality or motivational factors related to the decision to join this self-help group. Some authors have reported that alcoholics who attend AA are typically more

Table 4 Correlation matrix of the variables included in the multivariate analyses (Pearson's r, Phi, point-biserial)

Variables	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)	(9)	(10)	(11)	(12)	(13)	(14)
(1) OCDS	-													
(2) Age at the beginning of each trial	-0.22**	-												
(3) Race (white)	ns	ns	-											
(4) Family alcoholism	0.20**	ns	ns	-										
(5) SADD	0.70**	-0.22**	ns	0.23**	-									
(6) Smoking	ns	ns	0.13*	ns	ns	-								
(7) Time since the regular drinking onset age (in years)	ns	0.60**	ns	0.14*	ns	ns	-							
(8) Time since the problem drinking onset age (in years)	ns	0.40**	ns	ns	ns	ns	0.75**	-						
(9) Preferred beverage (spirits)	0.16**	ns	ns	ns	0.23**	ns	ns	ns	-					
(10) Quantity of ethanol per day	0.37**	-0.19**	ns	0.15*	0.35**	ns	-0.18**	-0.16*	0.15*	-				
(11) HDRS	ns	ns	ns	ns	ns	ns	0.18**	0.14*	ns	ns	-			
(12) Marital status (married)	-0.22**	0.19**	ns	ns	-0.26**	ns	0.14*	ns	ns	-0.15*	ns	-		
(13) Monthly income	ns	ns	ns	ns	-0.16**	ns	ns	ns	-0.14*	ns	-0.15*	ns	-	
(14) Previous treatments for alcoholism	ns	ns	ns	ns	ns	ns	ns	ns	ns	ns	0.16**	ns	ns	-

* $p < 0.05$; ** $p < 0.01$; ns: not significant;
OCDS: Obsessive Compulsive Drinking Scale; SADD: Short Alcohol Dependence Data; HDRS: Hamilton Depression Rating Scale.

sociable and affiliative, more guilty over past behavior, physically healthier, and more socially stable.[30] Conversely, other authors have affirmed that attendance at AA is more common among racial and ethnic minority groups, those with lower incomes, and those with unstable employment.[31] Although these generalizations can be problematic and doubtful, some characteristics attributed to AA participants have a certain level of acceptability, given the inherent characteristics of self-help groups. In fact, participating in AA was not an obligatory condition to partake in any of our trials, despite the encouragement given by researchers. This fact could mean that the most motivated and affiliative patients decide to participate in AA with the goal of improving their coping skills and changing their friendship networks.[32] Other authors suggest that success in AA is associated with frequent and continued attendance and not with motivation per se.[33]

Active medications did not influence treatment retention in the present study. Other studies have already shown that treatment with opioid antagonists,[34] topiramate,[35] and ondansetron, alone or in combination with naltrexone,[36,37] was not associated with increased retention in treatment, compared with placebo. Furthermore, even combinations of two medications for alcoholism have not shown effects on retention in treatment compared with individual pharmacotherapies alone.[38]

Although craving is an important factor to be measured and investigated at baseline and during treatment, our study was not able to show that it is a strong predictive factor of retention, at least when craving intensity was computed at baseline only. In reality, craving is not a stable state but rather depends on other variables that can be modified during treatment, such as mood, stress, substance-using status, environmental cues, etc. Nevertheless, other variables significantly correlated with craving, such as age and preferred beverage, were significantly associated with treatment retention.

Despite the heterogeneity of our clients, many therapeutic programs offer only a single type of treatment. With this "one size fits all" model, variations in retention have been commonly attributed to client factors or characteristics. Although this belief might be true to some extent, health services should broaden the scope of services offered to meet the heterogeneous needs of clients and identify treatment practices and therapies that improve retention. Information about patients' characteristics linked to noncompliance or dropout should be used to render treatment programs more responsive and attractive, combining pharmacologic agents with more intensive and diversified psychosocial interventions. Certain approaches, such as compliance enhancement therapy and motivational interviews, can be effective options when combining adjunctive interventions for randomized clinical trials.[39] Strategies to improve motivation are of paramount importance in different treatment programs, and they will be taken into account in future research by our group.

There were several weaknesses in this present study, including the following:

(1) There were no other psychotherapeutic procedures associated with the pharmacological treatments, which could have increased the retention of the patients.
(2) The number of dropouts was high in both trials, probably as a result of their designs, which allowed patients to follow the standard community-based programs of treatment, without norms to increase patient retention. Although this approach to trial design, which allows for normal life events to influence trial outcomes, probably enhances external validity, it can lead to considerable difficulties in interpreting data, such as motives for relapse and premature discontinuation of follow-up.

(3) Additionally, our service is tertiary, and many severe cases are referred to it. This fact can be verified by the enormous quantity of ethanol consumed by our subjects. It is difficult to generalize our findings to a less severely alcoholic population.
(4) Our research did not include women. Some studies have shown that sex differences exert different influences on retention treatment and craving.[40]
(5) The dosage of ondansetron tested (16 mg/day) was higher than the dosages usually investigated by other studies. This fact might have compromised this study's comparability to other studies.
(6) Our trials limited the examination of AA participation to the frequency and regularity of meeting attendance, which failed to capture the breadth of involvement in the program.
(7) Although OCDS was measured at three time points (at baseline, at the sixth week, and at the twelfth week) in each double-blind study, we only evaluated the effect on treatment retention of OCDS measured at baseline, due to some of the participants having discontinued the treatment before the sixth week. In this study, our aim was to investigate treatment retention in general, without taking into account the different times at which dropouts occurred.

Disclosures

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** Modest*

*** Significant*

**** Significant. Amounts given to the author's institution or to a colleague for research in which the author has participation, not directly to the author.*

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