Clinical Factors Associated with Relapse in Male Alcohol Dependents During Six-Month Follow-up

Cüneyt Evren[1], Rabia Cetin[1], Mine Durkaya[1], Ercan Dalbudak[1]

ÖZET:

Erkek alkol bağımlılarında altı aylık takip süresinde rölaps ile ilişkili klinik etmenler

Amaç: Bu çalışmanın amacı erkek alkol bağımlılarında yatarak tedavi sonrası 6 ay içinde alkol kullanımının rölapsı ile ilişkili etmenleri değerlendirmektir.
Yöntem: İlk değerlendirme ardışık olarak servise yatırılmış 156 erkek alkol bağımlısı hastadan oluşmaktaydı. Bu hastalardan 107 tanesi yatarak tedavilerinden 6 ay sonra görüşmeye müsaitti. Hastalar yatarak tedavi sırasında Belirti Tarama Listesi 90 - Gözden Geçirilmiş Formu (SCL-90-R), Michigan Alkolizm Tarama Testi (MATT) ile ve taburculuklarından 6 ay sonra Beck Depresyon Envanteri (BDE), Beck Anksiyete Envanteri (BAE), AMATEM Tedavi için Motivasyon Ölçeği (ATMÖ) ve PENN Alkol Aşerme Ölçeği (PAAÖ) kullanılarak değerlendirildiler.
Bulgular: Yatarak tedavi gören 107 alkol bağımlısı hastanın %53.3'ünde (n=57) alkol kullanımının yinelediği şeklinde değerlendirilmiştir. Şu anki yaş, düzenli alkol kullanımına başlama yaşı, eğitim süresi, evlilik ve çalışma durumu gruplar arasında farklılık göstermedi. Ortalama MATT, ATMÖ'nin sorunların farkında olma alt ölçeği ve SCL-90-R'nin genel belirti indeksi de gruplar arasında anlamlı farklılık göstermedi. Depresyon, anksiyete ve aşerme puanları ise rölaps gösteren grupta yüksek ATMÖ'nin "tedavi motivasyonu ve değişime hazır olma" alt ölçeği bu grupta düşük bulundu. Rölaps gösteren grupta daha az poliklinik kontrolü, daha az ayaktan terapi programına katılımı, risklerden korunmak için daha az sosyal çevre değişikliği ya da aşerme için daha az düzenli ilaç kullanımı saptanırken, bu grupta 6 ay içinde daha fazla yaşam olayı gözlendi. Aşerme şiddeti (özellikle 5. madde), sosyal çevre değişikliği yapmama ve 6 ay içinde yaşam olayı olması alkol bağımlılarında yatarak tedavi sonrası 6 ay içinde belirtilerin rölapsı ile ilişkili bulunmuştur.
Sonuç: Aşerme 6. ayda rölaps ile ilişkili temel etken olarak görülmektedir. Ayrıca aşermeyi arttıran etkenler (örn., riskli çevreyi değiştirmeme, remisyon sırasında yaşam olayı tecrübe etme ve yüksek düzeyde olumsuz duygulanım) ayık alkol bağımlısını rölaps riski içine sokabilir. Aşerme giderici ilaçlarla birlikte ayaktan tedavi programına düzenli katılım kişiyi yaşam değişikliği için motive edebilir ve yaşam olaylarıyla nasıl baş edeceğini öğretebilir.

Anahtar sözcükler: Alkol bağımlılığı, aşerme, rölaps, terapi

Klinik Psikofarmakoloji Bülteni 2010;20:14-22

ABSTRACT:

Clinical factors associated with relapse in male alcohol dependents during six-month follow-up

Objective: Aim of this study was to evaluate the clinical factors associated with relapse to alcohol use during six-month after inpatient treatment in male alcohol dependents.
Method: Participants were 156 consecutively admitted male alcohol dependents. Among these patients 107 were available to examine 6 months after inpatient treatment. Patients were administered the Symptom Checklist-Revised-90 (SCL-90-R), and Michigan Alcoholism Screening Test (MAST) at baseline and the Beck Depression Inventory (BDI), the Beck Anxiety Inventory (BAI), AMATEM Motivation for Treatment Scale (AMTS), and the PENN Alcohol Craving Scale (PACS) six-month later at follow-up.
Results: Among 107 alcohol dependent inpatients 53.3% (n=57) were considered as relapsed to alcohol use. Current age, age at regular alcohol use, duration of education, and marital and employment status did not differ between groups. Mean scores of MAST, awareness of problems of AMTS and GSI also did not differ significantly between groups, whereas depression, anxiety and craving scores were higher and "treatment motivation and readinees to change" subscale of AMTS was lower in relapsed group. Relapsed group had less outpatient clinic control, attendance to outpatient treatment program, change in social milieu to protect themselves and use of medicine for craving but experienced more life stressors during six-month follow-up. Severity of craving (particularly 5th item), not changing social milieu and life stressors experienced during six-month follow-up predicted relapse in alcohol dependents after inpatient treatment.
Conclusions: Craving seems to be the main factor associated with relapse. Also factors that increase craving (i.e., not changing risky environment, experiencing life stressor during remission and higher negative affect) may put sober alcohol dependents at risk of relapse. Adjunct anti-craving medications, regular attendance to the outpatient treatment may motivate patients for life changes and teach them how to cope with life-stressors.

Key words: Alcohol dependence, craving, relapse, therapy

Bulletin of Clinical Psychopharmacology 2010;20:14-22

[1]Bakirkoy State Hospital for Mental Health and Neurological Disorders, Alcohol and Drug Research, Treatment and Training Center (AMATEM), Istanbul, Turkey

Yazışma Adresi / *Address reprint requests to:* Cuneyt Evren MD, Icadiye Cad. Mentes Sok., Selcuk Apt. 1/17 Kuzguncuk, 34674 Uskudar, Istanbul-Turkey

Telefon / *Phone*: +90-216-341-0609

Faks / *Fax*: +90-216-660-0026

Elektronik posta adresi / *E-mail address:* cuneytevren@yahoo.com cuneytevren@hotmail.com

Kabul tarihi / *Date of acceptance:* 26 Ocak 2010 / January 26, 2010

Bağıntı beyanı: C.E., R.C., M.D, E.D.: yok.

Declaration of interest: C.E., R.C., M.D, E.D.: none.

INTRODUCTION

Among treated patients with alcohol use disorders, short-term remission rates vary between 20 to 50%, depending on the severity of the disorder and the criteria for remission (1,2). Studies suggest that among these individuals, more frequent and heavier alcohol consumption and more psychological and social drinking

problems are associated with a lower likelihood of remission (3,4).

Relapse is a multi-factorial phenomenon and most likely to result from a combination of various factors (5). Variables involved in relapse include the individual characteristics of the patient, the drug and environmental reinforcers (5,6). Among treated individuals, more severe alcohol-related problems and depressive symptoms, lack of self-efficacy, poor coping skills and readiness for change have been associated with relapse in short-term (6-9). Compared to individuals who obtain help, those who do not are less likely to achieve long term remission and subsequently are more likely to relapse (10). A risk factor score composed of these indicators could serve as an early warning sign of the potential for relapse after remission and perhaps trigger preventive or more intensive continuing care (10).

One feature noted before relapse in some abstinent patients is craving for alcohol, which may contribute to the risk of relapse (5). Higher levels of craving assessed in role play and cue reactivity are known as a risk factor for a worse outcome in alcoholism (6,11,12). O'Connor et al. (13) have reported a higher dropout rate during alcohol withdrawal among outpatients with an increased craving. Among patients in outpatient treatment program, craving predicted both relapse during the treatment phase and heavy relapse 12-month after completion of the treatment (5). Behavioral models attempt to explain the nature of craving although no single model accounts for all aspects of craving. The reinforcement model postulates that alcohol can improve mood or reduces unpleasant mental states such as anger, frustration or stress. In alcoholics an unconscious learning process (reinforcement) can lead to alcohol drinking in order to re-experience the positive mental state (14).

Reviewing laboratory, clinical, family, and prospective studies, Kushner et al. (15) concluded that anxiety disorder and alcohol disorder could initiate each other, and that the former can contribute to the maintenance of and relapse into pathological alcohol use. Driessen et al. (16) concluded that severe trait anxiety persisting after 3 weeks of abstinence, co-morbid depressive and/or anxiety disorders, and combinations of these with moderate or severe current anxiety and depressive states are associated with increased risk of relapse in alcoholics. Findings on the effect of depressive mood on the likelihood of returning to drinking are contradictory (17). For example, according to Heinz et al. (18) and Driessen et al. (16), depressed mood increases the relapse risk of abstinent alcoholics. Depressive symptoms were the most frequently endorsed relapse determinants reported retrospectively by men treated for alcohol addiction (19). On the other hand, Greenfield et al. (20) reported that depressive mood, measured by the Beck Depression Inventory, did not prospectively predict relapse in women or men.

The question of which factors predict relapse is therefore an important one, since by understanding what such factors are, strategies for minimizing their effects can be developed. Listed among the many predictors of whether or not alcoholism relapse will occur are life events, mood states, the existence of self-efficacy, coping behaviors, and social support resources (6,8,21). Best to our knowledge this is the first study conducted among Turkish alcohol dependents to evaluate the predictors of relapse in a follow-up study. In this current study, we aimed to evaluate the clinical factors associated with relapse to alcohol use during six-month follow-up after inpatient treatment in male alcohol dependents.

METHODS

Subjects

The study cohort was recruited at the Bakirkoy State Hospital for Psychiatric and Neurological Diseases, Alcohol and Drug Research, Treatment and Training Center (AMATEM) in Istanbul between January 2007 and January 2009. AMATEM is a specialized center for substance use disorders with 85 inpatient beds, and accepts patients from all over Turkey. The study protocol was approved by the Ethical Committee of the Hospital . Patients provided written informed consents after the study protocol was thoroughly explained.

One hundred and eighty consecutively admitted alcohol-dependent inpatients without history of any other substance abuse were enrolled. All participants fit the DSM-IV diagnostic criteria for alcohol dependence. Excluding criteria were illiteracy, mental retardation or cognitive impairment, and comorbid psychotic disorder. Five patients were excluded due to illiteracy and three patients due to cognitive deficits. Although none of the

patients refused to participate in the study, 16 patients were excluded because they left some parts of the scales unfilled, did not return the forms or left the treatment program prematurely; i.e., before filling the forms. A total of 156 alcohol-dependent inpatients participated in the study. Interviews with the study group were conducted after detoxification period, i.e., 4-6 weeks after the last day of alcohol use.

Six months later, each of these 156 participants were called with phone to invite them to the clinic for a second interview. It was possible to reach 139 (89.1%) patients by phone, among which 55.4% relapsed during the six months. Nevertheless, second evaluation only was possible with 107 (68.6%) patients, because they could not or they did not want to come to the clinic for several reasons.

Assessments

All patients were assessed by using a semi-structured socio-demographic form both at baseline and at six-month follow-up. The diagnosis of alcohol or drug dependence in each participating patient based on the clinical examination, a screening interview based on the Structured Clinical Interview for DSM-IV (SCID-I) (22), Turkish version (23), conducted by trained interviewer (CE).

Symptom Check List-Revised-90 (SCL-90-R): Psychopathologic symptoms were assessed with widely used 90-item Symptom Checklist-Revised-90 (SCL-90-R), a self rating inventory (24). The total score and the global severity index (GSI) were considered as a measure of overall psychopathology. The SCL-90-R is a reliable and valid measure of psychopathology and is widely used in researches. In the present study Turkish version of the inventory was used (25). Cronbach's alpha was found 0.98 in the present study.

Michigan Alcoholism Screening Test (MAST). The MAST was used in assessment of the severity of dependence (26). It was developed as a rapid and effective screening for lifetime alcohol-related problems and alcoholism for a variety of populations. MAST consists of 25 brief True-False items that are self-administered in approximately 10 minutes. Scoring is accomplished after reverse scoring 4 of the 25 items and assigning weighed scores. These weighed scores are then summed; the sum represents a total score reflecting severity of alcohol-related problems. Turkish version of the MAST is valid and reliable for screening severity of dependency of both alcohol and drug dependent patients (27). The Cronbach's alpha was found 0.73 in the present study.

Beck Depression Inventory (BDI) and Beck Anxiety Inventory (BAI): Symptoms and severity of depression were evaluated by using the Beck Depression Inventory (BDI) (28), Turkish version (29) and symptoms and severity of anxiety were evaluated by the Beck Anxiety Inventory (BAI) (30), Turkish version (31). Cronbach's alfa was found 0.94 for BDI and 0.95 for BAI in the present study.

Penn Alcohol Craving Scale (PACS): Craving of the individuals were evaluated with Penn Alcohol Craving Scale (PACS) (32). PACS is a 5 item self-rating scale for evaluating severity of craving (frequency, intensity, duration, resistance and general craving) in the past week. For each items scores range from 0 to 6. Thus the total score of craving is 30. PACS showed high validity and high reliability (32). Turkish version of PACS was used in the present study, which was found to be valid and reliable among male inpatient alcohol dependents (33). Cronbach's alfa was found 0.96 in the present study.

AMATEM Motivation for Treatment Scale (AMTS): To evaluate the treatment motivation, items selected from the Treatment Motivation Questionnaire (TMQ) (34) and the Stages of Change Readiness and Treatment Eagerness Scale (SOCRATES) (35), together with items added by Evren et al. (36), a 33 item self-rating scale was developed. Repeated factorial analysis showed that the scale with 18 items and 2 factor solution was appropriate. First factor (Awareness of problems) consisted of 10 items and second factor (Treatment motivation and readinees to change) consisted of 8 items. In alcohol dependents the internal consistency coefficient (Cronbach's alpha) was 0.93 for first factor, 0.93 for second factor and 0.94 for EMTS, which found to be valid and reliable scale in Turkish alcohol dependents (36).

Statistical Analysis

The statistical package SPSS 15.0 for Windows (SPSS Inc., Chicago, IL) was used for all the analyses. Categorical variables were compared with chi-square test. We used Student's t test for independent samples to compare continuous variables. Taken relapse status as

dependent variable, two Forward Logistic Regression models were performed. In first model, age onset of regular alcohol use, global severity index of SCL-90-R, MAST score, depression, anxiety, therapy at follow up, treatment motivation, social change and trauma during follow up were independent variables. In second model the same variables were taken as independent variables. Only exception was PACS score, instead of which PACS items were taken as independent variables. For all statistical analysis p values were two-tailed and differences were considered significant at $p<0.05$.

RESULTS

Among 156 alcohol dependent inpatients 107 (68.6%) were available for interview at the end of six months. Fifty seven (53.3%) of these patients were considered as relapsed to alcohol use during the six months, whereas 50 (46.7%) were still in remission. Mean age, duration of education, age at regular alcohol use, marital and employment status did not differ between the relapsed and remission groups (Table 1).

Mean scores of depression, anxiety and craving at second interview were higher in relapsed group, whereas severity of psychiatric symptoms and alcohol related problems at baseline interview did not differ between relapsed and remission groups. Although "Awareness of problems" factor of AMTS was lower in relapse group, difference was not significant. "Treatment motivation and readinees to change" factor was significantly lower in relapsed group (Table 2).

The relapsed group had less regular outpatient clinic control, less regular attendance to outpatient treatment program, made less changes in social milieu to protect themselves and they did not use medicine for craving but they experienced more life stressors during six-month follow-up (Table 3). Severity of craving (PACS score), not making changes in social milieu and experiencing a life stressor during follow-up period predicted relapse to alcohol in Forward Logistic Regression model. Age at regular alcohol use, global severity index (GSI) of SCL-90-R, MAST score, depression, anxiety, motivation for treatment, outpatient therapy at follow up, social change and trauma during follow-up were independent variables

Table 1: Sociodemographic variables.

	Remission		Relapse				
	N=50	%	N=57	%	$\chi 2$	df	P
Marital status					2.21	2	0.33
Married	31	62.0	38	66.7			
Divorced, Widow, Separate	4	8.0	8	14.0			
Single	15	30.0	11	19.3			
Employment status					3.46	3	0.33
Without employment	13	26.0	20	35.1			
With employment	24	48.0	17	29.8			
Part time	5	10.0	6	10.5			
Retired	8	16.0	14	24.6			
Age (mean±SD)	46.18±9.75		43.60±8.39		t=1.47		0.14
Duration of education (mean±SD)	10.02±4.07		9.60±3.94		t=0.55		0.59
Age onset of regular substance use (mean±SD)	26.74±8.60		26.26±8.56		t=0.29		0.78

Table 2: Scale scores among alcohol dependent men according to the relapse status at 6 month.

Scale scores	Remission (n=50) mean±sd	Relapse (n=57) mean±sd	t	P
SCL-90-R global severity index	1.38±0.86	1.51±0.85	-0.82	0.42
Michigan Alcoholism Screening Test (MAST)	26.56±9.90	28.72±10.30	-1.10	0.27
Beck Depression Inventory	5.18±7.92	14.02±11.29	-4.73	<0.001
Beck Anxiety Inventory	5.36±6.89	13.40±13.24	-4.01	<0.001
PENN Alcohol Craving Scale (PACS)	4.36±5.33	15.32±10.88	-6.74	<0.001
AMTS Awareness of problems	37.88±8.53	34.32±12.69	1.72	0.088
AMTS Treatment motivation and readinees to change	39.72±7.57	35.26±10.44	2.55	0.012

AMTS: AMATEM Motivation for Treatment Scale

Table 3: Treatment related variables in 6 months.

	Remission		Relapse				
	N=50	%	N=57	%	$\chi 2$	sd	P
Polyclinic control					9.41	2	0.009
No	21	42.0	37	64.9			
Irregular	12	24.0	14	24.6			
Regularly	17	34.0	6	10.5			
Compliance to Outpatient Treatment Program*	30	60.0	17	29.8	9.85	1	0.002
Social milieu change **	39	78.0	27	47.4	10.57	1	0.001
Trauma during 6-month follow-up ***	1	2.0	10	17.5	6.98	1	0.008
Compliance to Medication					17.33	2	0.001
Non-compliance	8	16.0	3	5.3			
Partialy compliance	12	24.0	36	63.1			
Full compliance	30	60.0	18	31.6			

Odds Ratio (95% Confidence Interval): *0.29 (0.13-0.63), **0.25 (0.11-0.59), *** 10.43 (1.28-84.65)

Table 4: Determinants of relapse in Forward Logistic Regression models in alcohol dependent men (n=107).

Relapse during 6 months	B	S.E.	Wald	df	P	Odds Ratio	95.0% Confidence Interval
Model 1							
PACS	0.156	0.037	18.028	1	<0.001	1.169	1.088-1.256
Social change during follow-up	1.442	0.539	7.166	1	0.007	4.230	1.472-12.162
Life stressor during follow-up	-2.336	1.168	4.005	1	0.045	0.097	0.010-0.953
Model 2							
PACS-5th item (General craving)	0.836	0.196	18.101	1	<0.001	2.307	1.570-3.391
Social change during follow-up	1.392	0.544	6.540	1	0.011	4.025	1.384-11.701
Life stressor during follow-up	-2.427	1.232	3.885	1	0.049	0.088	0.008-0.986

Model 1: Age onset of regular alcohol use, global severity index of SCL-90-R, Michigan Alcoholism Screening Test, depression, anxiety, therapy at follow up, treatment motivation, social change and trauma during follow up were independent variables. Model 2: PACS items were taken as independent variables instead of total PACS score. Other than this, independent variables were the same as Model 1.

in this model. These variables were selected because most of them were related with relapse. GSI of SCL-90-R and MAST score were not related with relapse, but since we believe that severity of psychiatric symptoms and alcohol related problems were important variables that may be associated with relapse, we also included these variables as independent ones. Since PACS score was one of the main predictors of relapse in this model, taken each PACS items instead of total score of PACS as independent variables, we conducted a second Forward Logistic Regression analyses. In this model 5th item of PACS (general rating of craving), not making changes in social milieu and experiencing a life stressors during follow-up predicted relapse to alcohol use (Table 4).

DISCUSSION

Among those who were available for interview at the end of 6 month (107, 68.6%), fifty seven (53.3%) of them were considered as relapsed to alcohol use during the six-month follow-up. This rate was consistent with previous studies which found 50-80% relapse rates for short term treatment (1,2) and 57% for the 12 months after treatment (37). The main finding of the present study is that craving and factors that are related with craving is associated with relapse at six-month follow-up after inpatient treatment. Different subtypes of patients could have different mechanisms at the basis of their alcohol craving (38). Therefore, different risk factors may cause craving as a final pathway for relapse. Patients with increased craving dropped out significantly more often during the treatment phase (37). In previous studies craving at the end of the treatment predicted alcohol use at 3-month follow-up (39) at the 6-month follow-up (5) and at 12-month follow-up (5). Also relapsed patients showed higher craving scores than improvers and abstainers (5). As a consequence, patients with increased craving should be treated more intensively by using additional relapse prevention approaches which may help the patient to recognize cues that lead to drinking (5). Higher craving is related with

higher severity of psychopathology, including negative affect (40,41). Patients should develop strategies to cope with high-risk situations such as negative emotional states and interpersonal conflicts (42). Other finding of the present study is that, although PACS is an easy use and time saving instrument, even simply using "general craving" item (5th item) of PACS can give important information about individuals craving status and help to estimate the course of these individuals.

Previous research has shown that exposure to stress/ negative affect and to alcohol cues can each increase alcohol craving and relapse susceptibility in alcohol-dependent individuals (43). Stress is an important factor known to increase alcohol relapse risk (44). Alcoholics experiencing highly threatening or chronic psychosocial stress following treatment are more likely to relapse than abstaining individuals not experiencing such stress, which is also called the stress-vulnerability model of relapse (8). This was supported by findings of the present study. In previous study improvement in psychosocial domains (e.g., coping skills, social networks, perceived ability to tolerate relapse-risk situations) enhanced the ability of these men to remain abstinent despite severe stress (8). Findings of previous studies supported the idea that the likelihood of relapse rises in the absence of personal and social resources that reflect maintenance factors for stable remission (10). These findings highlight the importance of cognitive and behavioral interventions for increasing improvement in these psychosocial domains (8). Indeed in present study regular participation to outpatient treatment program (both psychotherapy and pharmacotherapy) after discharge from hospital and making social changes that are needed to decrease the risk of relapse seemed to protect alcohol dependents from relapse. Sinha et al., (45) suggested that treatments targeting decreases in stress and alcohol cue-induced craving and regulation of stress responses could be of benefit in improving alcohol relapse outcomes.

In treated samples, women and older, married and better-educated individuals tend to experience better short-term outcomes (3,46,47). Nevertheless, a combination of various factors with different impact may cause relapse, and probably there may be no single factor (5). In the present study sociaodemographic factors did not differ between groups, suggesting that other risk factors are more important in our sample. Our sample included only male patients, thus sociodemographic variables as a risk factors may change across genders. Not only sociodemographic but also other risk factors may differ between genders. For initial post-treatment relapses, women were more likely to have relapses due to negative affect, and men were more likely to have relapses due to social pressure (48).

Among treated individuals, more frequent and heavier alcohol consumption and more psychological and social drinking problems are associated with a lower likelihood of remission (3,4,49). In contrast with this severity of alcohol related problems evaluated with MAST did not differ between groups. Since MAST is a self-rating scale we mat speculate that the perception not the severity of problems did not differ between groups. Consistent with this, "awareness of problems" factor of AMTS did not differ significantly between groups and "treatment motivation and readinees to change" was significantly lower in relapsed group. It is logical to expect minimization of alcohol related problems in those with lower treatment motivation and readiness to change. Assessment of help-seekers' motivation and readiness for change may help target high-risk individuals for interventions to enhance and maintain participation in treatment (50). Results of previous studies demonstrated a relationship between pretreatment readiness for change and both the decision to drink and to engage in recovery activities; however, it appeared that, once drinking begins, variables other than pretreatment readiness for change influence frequency and quantity of alcohol consumption (51).

Alcohol craving and negative affect, which are associated, both have been postulated as important predictors of relapse in patients with alcohol dependence (52). Results of previous study indicated that a favorable outcome of socially stable alcohol-dependent patients and patients with a lower degree of depression, anxiety and craving in an intensive outpatient rehabilitation program (53). These findings were supported in the present study. The effects of anxiety and depressive symptoms on relapse might occur several ways. It may reduce energy needed to refrain from alcohol use. Feeling worse during abstinence due to depression than when using alcohol may reduce motivation to continue abstinence efforts. Depression may lead to self-medication. The 'self-medication hypothesis' suggests that the pharmacological and/ or psychological effects of alcohol reduce the aversive anxiety symptoms, thereby increasing persistent

and escalating use via negative reinforcement. Aspects of anxiety and depression may become conditioned cues for alcohol use, continuing to prompt alcohol cravings during abstinence (54,55). Negative affect relapses may occur in both gender but predictors may differ. For men, negative affect relapses were predicted by the Beck Depression Inventory score, whereas for women, negative affect relapses were predicted by the Alcohol Dependence Scale score (48).

There are several limitations for our findings. First, we have not examined biological markers (CDT or GT) nor collected reports of collateral informants, but we considered that the patients' self-reports and information from relatives would be valid. All patients were personally interviewed and all patients were well known by the same interviewer (E.D.). Several studies have shown a high validity and high reliability of self-report data of alcohol-dependent patients in treatment compared to toxicological analyses of blood or collateral informant reports (56,57).

Craving seems to be main factor related with relapse. Results of our study indicate that measurement of craving with the PACS, even "general craving" item of PACS, can be a useful tool to predict subsequent drinking during outpatient treatment, and may be useful in monitoring patients during treatment to identify individuals at risk for relapse. Maybe those patients with elevated craving scores who are at a higher risk for relapsing would benefit from intensified aftercare and of additional anticraving medication such as naltrexone or acamprosate (58,59). Also factors that may increase craving (i.e., not changing risky environment, experiencing life stressor during remission and negative affect) may put sober alcohol dependents at the risk of relapse. This study highlights the importance of cognitive and behavioral interventions for increasing improvement in these psychosocial domains (8). Results of a meta-analysis indicated that relapse prevention, which has become a widely adopted cognitive—behavioral treatment intervention for alcohol, smoking, and other substance use, was generally effective, particularly for alcohol problems, when combined with the adjunctive use of medication, and when evaluated immediately following treatment (60). Thus, in conjunction with anti-craving medications, regular attendance to the outpatient treatment program may motivate patients to cope with alcohol cravings, to make life changes and may teach them how to cope with life-stressors.

References:

1. Miller WR, Walters ST, Bennett ME. How effective is alcoholism treatment in the United States? J Stud Alcohol 2001;62:211–220.
2. Monahan S, Finney J. Explaining abstinence rates following treatment for alcohol abuse. A quantitative synthesis of patient, research design, and treatment effects. Addiction 1996;91:787–805.
3. McLellan AT, Alterman AI, Metzger DS, Grissom GR, Woody GE, Luborsky L, O'Brien CP. Similarity of outcome predictors across opiate, cocaine, and alcohol treatments: Role of treatment services. J Consult Clin Psychol 1994;62:1141–1158.
4. Booth BM, Curran GM, Han X. Predictors of short-term course of drinking in untreated rural and urban at-risk drinkers: effects of gender, illegal drug use, and psychiatric comorbidity. J Stud Alcohol 2004;65:63–73.
5. Bottlender M, Soyka M. Impact of craving on alcohol relapse during, and 12 months following, outpatient treatment. Alcohol Alcohol 2004;39:357-361.
6. Miller WR, Westerberg VS, Harris RJ, Tonigan JS. What predicts relapse? Prospective testing of antecedent models. Addiction 1996;91:155–171.
7. Yates WR, Booth BM, Reed DA, Brown K, Masterson BJ. Descriptive and predictive validity of a high-risk alcoholism relapse model. J Stud Alcohol 1993;54:645–651.
8. Brown SA, Vik PW, Patterson TL, Grant I, Schuckit MA. Stress, vulnerability, and alcohol relapse. J Stud Alcohol 1995;56:538–545.
9. Connors GJ, Maisto SA, Zywiak WH. Understanding relapse in the broader context of post-treatment functioning. Addiction 1996;91:S173–189.
10. Moss RH, Moss BS. Rates and predictors of relapse after natural and treated remission from alcohol use disorders. Addiction 2006; 101: 212–222.
11. Monti PM, Abrams DB, Binkoff JA, Zwick WR., Liepman MR, Nirenberg TD, Rohsenow DR. Communication skills training, communication skills training with family, and cognitive behavioral mood management training for alcoholics. J Stud Alcohol 1990;51:263–270.
12. Cooney NL, Litt MD, Morse PA, Bauer LO, Gaupp L. Alcohol cue reactivity, negative-mood reactivity, and relapse in treated alcoholic men. J Abnorm Psychol 1997;106:243–250.
13. O'Connor PG, Gottlieb LD, Kraus ML, Segal SR, Horwitz RI. Social and clinical features as predictors of outcome in outpatient alcohol withdrawal. J Gen Intern Med 1991;6:312–316.
14. Singleton EG, Gorelick DA. Mechanisms of alcohol craving and their clinical implications. In: Recent Developments in Alcoholism, Vol. 14: The consequences of alcoholism. Galanter, M. (ed.), 1998, 177–195. Plenum Press, New York, NY.

15. Kushner MG, Abrams K, Borchardt C. The relationship between anxiety disorders and alcohol use disorders: a review of major perspectives and findings. Clin Psychol Rev 2000;20:149–171.

16. Driessen M, Meier S, Hill A, Wetterling T, Lange W, Junghanns K. The course of anxiety, depression and drinking behaviours after completed detoxification in alcoholics with and without comorbid anxiety and depressive disorders. Alcohol Alcohol 2001;36:249–255.

17. Swendsen JD, Merikangas KR. The comorbidity of depression and substance use disorders. Clin Psychol Rev 2000;20:173–189.

18. Heinz A, Weingartner H, George D, Hommer D, Wolkowitz OM, Linnoila M. Severity of depression in abstinent alcoholics is associated with monoamine metabolites and dehydroepiandrosterone-sulfate concentrations. Psychiatry Research 1999; 89:97–106.

19. Strowing AB. Relapse determinants reported by men treated for alcohol addiction: the prominence of depressed mood. J Subst Abuse Treat 2000;19:469–474.

20. Greenfield SF, Weiss RD, Muenz LR, Vagge LM, Kelly JF, Bello JR, Michael J. The effect of depression on return to drinking: a prospective study. Arch Gen Psychiatry 1998;55:259–265.

21. Janowsky DS, Boone A, Morter S, Howe L. Personality and alcohol/substance-use disorder patient relapse and attendance at self-help group meetings. Alcohol Alcohol 1999;34:359-369.

22. First MB, Spitzer RL, Gibbon M, Williams JBW. Stuructured Clinical Interview for DSM-IV Axis I Disorders (SCID-I), Clinical Version. Washington D.C. and London: American Psychiatric Press, Inc, 1997.

23. Corapcioglu A, Aydemir O, Yildiz M, Esen A., Koroglu E. DSM-IV Eksen I Bozuklukları (SCID-I) için Yapılandırılmış Klinik Görüşme, Klinik Versiyon. Ankara. Hekimler Yayın Birliği, 1999. (in Turkish)

25. Dag I. Belirti tarama listesi (SCL-90-R) nin üniversite öğrencileri için güvenirliği ve geçerliği, (Reliability and validity of Symptom Check List-90-Revised among university students), Turkish Journal of Psychiatry 1991;2: 5-12. (in Turkish)

24. Derogatis LR. SCL-90: Administration, Scoring and Procedure Manual-II for the revised version, Tawson, Clinical Psychometric Research, 1983.

27. Coskunol H, Bagdiken I, Sorias S, Saygili R. Validity and reliability of the Michigan Alcoholism Screening Test (Turkish version). Aegean J Med 1995;34:15-18. (in Turkish)

26. Gibbs LE. Validity and reliability of the Michigan Alcoholism Screening Test: A review. Drug Alcohol Depend 1985;12: 279-285.

28. Beck AT, Ward CH, Mendelson M, Mock J, Erbaugh J. An inventory for measuring depression. Arch Gen Psychiatry 1961;4:561-571.

29. Hisli N. Reability and validity of Beck Depression Inventory among university students. Journal of Turkish Psychology 1989;7:3-13. (in Turkish)

30. Beck AT, Epstein N, Brown G, Steer RA. An inventory for measuring clinical anxiety: psychometric properties. J Consult Clin Psychol 1988;56:893-897.

31. Ulusoy M, Erkmen H, Sahin N. Turkish version of the Beck Anxiety Inventory: Psychometric properties; Journal of Cognitive Psychotherapy; An international quarterly 1998;12:163-172.

32. Flannery BA, Volpicelli JR, Pettinati HM. Psychometric properties of the Penn Alcohol Craving Scale. Alcohol Clin Exp Res 1999;23:1289-1295.

33. Evren C, Flannery B, Çelik R, Durkaya M, Dalbudak E. Penn Alkol Aşerme Ölçeği (PAAÖ) Türkçe Şeklinin Yatarak Tedavi Gören Erkek Alkol Bağımlısı Hastalarda Geçerliği ve Güvenirliği. Bağımlılık Dergisi 2008;9:128-134. (in Turkish)

34. Evren C, Saatçioğlu Ö, Dalbudak E, Danışmant BS, Çakmak D, Ryan RM. Tedavi Motivasyonu Anketi (TMA) Türkçe Versiyonunun Alkol Bağımlısı Hastalarda Faktör Yapısı, Geçerliği ve Güvenirliği. Bağımlılık Dergisi, 2006; 7: 117-122. (in Turkish)

35. Evren C, Dalbudak E, Cakmak D. Değişime Hazır Olma ve Tedavi İsteği Ölçeği (SOCRATES) Türkçe Versiyonunun Yatarak Tedavi Gören Erkek Alkol Bağımlısı Hastalarda Faktör Yapısı, Geçerliği ve Güvenirliği. Klinik Psikofarmakoloji Bülteni 2008;18:84-91. (in Turkish)

36. Cetin R. Alkol bağımlılarında travma sonrası stress bozukluğu ve kişilik özelliklerinin remisyona etkisi ve remisyonun tedavi motivasyonu ve aşerme ile ilişkisi. Tez Istanbul, 2009. (in Turkish)

37. Soyka M, Hasemann S, Scharfenberg CD, Löhnert B, Bottlender M. New possibilities in treatment and rehabilitation of alcohol-dependent patients — a catamnestic study on the efficiency of outpatient treatment programmes demonstrated by a model procedure. Nervenarzt 2003;74:226–234.

38. Addolorato G, Leggio L, Abenavoli L, Gasbarrini G; Alcoholism Treatment Study Group. Neurobiochemical and clinical aspects of craving in alcohol addiction: a review. Addict Behav. 2005;30:1209-1224.

39. Gordon SM, Sterling R, Siatkowski C, Raively K, Weinstein S, Hill PC. Inpatient desire to drink as a predictor of relapse to alcohol use following treatment. Am J Addict 2006;15:242-245.

40. Evren C, Durkaya M, Çelik R, Dalbudak E, Çakmak D, Flannery B. Yatarak tedavi gören erkek alkol bağımlısı hastalarda alkol aşermesinin aleksitimi ve dissosiyasyon ile ilişkisi. Anadolu Psikiyatri Dergisi 2009; 10:165-173

41. Evren C, Çetin R, Durkaya M, Dalbudak E, Çakmak D. Yatarak Tedavi Gören Erkek Alkol Bağımlısı Hastalarda Alkol Aşermesinin Travma Sonrası Stres Bozukluğu ve Genel Psikopatolojinin Şiddeti ile İlişkisi. NöroPsikiyatri Arşivi 2009; 46(1):3-7. (in Turkish)

42. Larimer ME, Palmer RS, Marlatt GA. Relapse prevention. An overview of Marlatt's cognitive-behavioral model. Alcohol Res Health. 1999;23:151-160.

43. Fox HC, Bergquist KL, Hong KI, Sinha R. Stress-induced and alcohol cue-induced craving in recently abstinent alcohol-dependent individuals. Alcohol Clin Exp Res 2007;31:395-403.

44. Sinha R. The role of stress in addiction relapse. Curr Psychiatry Rep 2007;9:388-395.

45. Sinha R, Fox HC, Hong KA, Bergquist K, Bhagwagar Z, Siedlarz KM.Enhanced negative emotion and alcohol craving, and altered physiological responses following stress and cue exposure in alcohol dependent individuals. Neuropsychopharmacology 2009;34:1198-208.

46. Ornstein P, Cherepon JA. Demographic variables as predictors of alcoholism treatment outcome. J Stud Alcohol 1985;46: 425–432.

47. Jarvis TJ. Implications of gender for alcohol treatment research: a quantitative and qualitative review. Br J Addict 1992;87: 1249–1261.

48. Zywiak WH, Stout RL, Trefry WB, Glasser I, Connors GJ, Maisto SA, Westerberg VS. Alcohol relapse repetition, gender, and predictive validity. J Subst Abuse Treat 2006;30:349-353.

49. Armor DJ, Meshkoff JE. Remission among treated and untreated alcoholics. Adv Subst Abuse 1983;3: 239–269.

50. Marlowe DB, Merikle EP, Kirby KC, Festinger DS, McLellan AT. Multidimensional assessment of perceived treatment entry pressures among substance abusers. Psychol Addict Behav 2001;15:97–108.

51. Isenhart CE. Pretreatment readiness for change in male alcohol dependent subjects: predictors of one-year follow-up status. J Stud Alcohol 1997;58:351-357.

52. Oslin DW, Cary M, Slaymaker V, Colleran C, Blow FC. Daily ratings measures of alcohol craving during an inpatient stay define subtypes of alcohol addiction that predict subsequent risk for resumption of drinking. Drug Alcohol Depend 2009;103:131-136.

53. Bottlender M, Soyka M. Efficacy of an intensive outpatient rehabilitation program in alcoholism: predictors of outcome 6 months after treatment. Eur Addict Res 2005;11:132-137.

54. Hasin D, Liu X, Nunes E, McCloud S, Samet S, Endicott J. Effects of major depression on remission and relapse of substance dependence. Arch Gen Psychiatry 2002;59:375-380.

55. Willinger U, Lenzinger E, Hornik K, Fischer G, Schönbeck G, Aschauer HN, Meszaros K; European fluvoxamine in alcoholism study group. Anxiety as a predictor of relapse in detoxified alcohol-dependent patients. Anxiety as a predictor of relapse in detoxified alcohol-dependent patients. Alcohol Alcohol 2002;37:609-612.

56. Mundle G, Ackermann K, Günthner A, Munkes J, Mann K. Treatment outcome in alcoholism - a comparison of self-report and the biological markers carbohydrate-deficient transferrin and gamma-glutamyl transferase. Eur Addict Res 1999;5:91-96.

57. Babor TF, Steinberg K, Anton R, Del Boca F. Talk is cheap: measuring drinking outcomes in clinical trials. J Stud Alcohol. 2000;61:55-63.

58. Boening JAL, Lesch OM, Spanagl R, Wolfgramm J, Narita M, Sinclair D, Mason BJ, Wiesbeck GA. Pharmacological relapse prevention in alcohol dependence: From animal models to clinical trials. Alcohol Clin Exp Res 2001;25 (Suppl.5):127 –131 .

59. Soyka M, Chick J. Use of acamprosate and opioid antagonists in the treatment of alcohol dependence: a European perspective. Am J Addict 2003;12 Suppl 1:S69-80.

60. Irvin JE, Bowers CA, Dunn ME, Wang MC. Efficacy of relapse prevention: a meta-analytic review. J Consult Clin Psychol 1999;67:563-570.