Original article:

A study of personality and neurobiological correlates of relapse in alcohol dependent in-patients

[1]Dr. Pankaj B. Borade, [2]Dr. SoniaMalhotra

[1]M.D., S.M.S. Medical College, Jaipur

[2]M.D., S.M.S. Medical College, Jaipur

Department(s) and Institution(s): Department of Psychiatry, S.M.S. Medical College, Jaipur

Corresponding author: Dr. Sonia Malhotra

Abstract:

Alcoholism is a very common diagnosis affecting persons of every social class and every country. Worldwide alcohol consumption causes 2,5 million deaths per annum (3.8 % of total) and 69.4 million (4.5 % of total) of Disability-Adjusted Life Years (DALYs), and is responsible for many health and social problems according to information provided by the World Health Organization (2010). It is a major cause of morbidity and mortality, with well-established deleterious effects on many organ systems, including the central nervous system.

This study was planned with an aim to recognize the personality and neurological correlates of relapse in alcohol dependent patients. The study does find a significant difference in the expression of depression, anxiety, compulsion and psychoticism, among personality correlates associated with relapse in alcohol dependent patients. Though, finding the trend of these correlations were beyond the scope of this study.

Introduction

Alcoholism is a very common diagnosis affecting persons of every social class and every country. Worldwide alcohol consumption causes 2,5 million deaths per annum (3.8 % of total) and 69.4 million (4.5 % of total) of Disability-Adjusted Life Years (DALYs), and is responsible for many health and social problems according to information provided by the World Health Organization (2010)[1]. It is a major cause of morbidity and mortality, with well-established deleterious effects on many organ systems, including the central nervous system[2].

In recent years, Substance Use Disorders (SUDs), or addictions to psychoactive substances, have often been characterized as chronic brain diseases that result from long-term exposure to psychoactive drugs to the brain[3,4]. Several neuropsychological changes have also been described which may be related to frontal lobe dysfunction.

These changes include impaired planning, organization, abstracting and problem solving[5,6]. Some neurocognitive impairments appear to be general to all SUDs whereas other dysfunctions may be more specifically linked to a certain substance of abuse[7]. Although neurocognitive impairments have been well profiled in various substance use disorders, much less is known about the persistence of such deficits. Despite considerable research, there are conflicting opinions regarding alcohol use and its

association with cognitive dysfunction[8-11]. There is consensus that alcohol intoxication often results in short-term dysfunction across a range of cognitive domains in healthy volunteers[12-14]. The extent to which chronic alcohol use is associated with cognitive impairments, however, remains less clear. Importantly, from a clinical perspective, successful recovery of cognitive impairments has been found to predict treatment response and stable abstinence[15]. A study suggested that the early recognitionof mild and moderate degrees of alcohol-relatedbrain damage is important, since if measures aretaken to reduce alcohol consumption at that stage,more serious social and physical deteriorationmight be averted[16].

Although neurological abnormalities among patients with alcohol dependence are well documented, such reports have largely confined themselves to 'hard' signs which have predictive localizing power, usually referable to specific lesions of nuclei, tracts or nerves. 'Soft' signs, although abnormal, are so called because they do not have such predictive power.

Included within the concept of 'soft'signs are phenomena such as astereognosis, primitive reflexes, dysdiadochokinesia, mirror phenomena, sensory extinction and cortical sensory loss. While the clinical significance of neurological soft signs is unclear, they are widely regarded as an indicator of non-specific brain damage[17], and their presence reflects dysfunction in the areas of motor co-ordination, integrative sensory function and ordering of complex motor tasks.

Among the psychological correlates of alcoholism, personality traits derived from impulse control disorders like impulsivity and aggression as well as those associated with psychological states often preceding onset of alcoholism like depression and anxiety have been described as characteristics of this disorder[18-22]. The wide literature on the relationship between Eysenck's dimensional model of personality and the use of drugs, alcohol and tobacco confirms that psychoticism is a key personality factor in this area[23]. Another personality construct, whose relation to substance use is broadly explored, is that of sensation seeking. Sensation seeking appears to be a neurochemically based personality trait characterized by a need for stimulation, making individuals relatively high in sensation seeking more vulnerable to substance abuse and more susceptible to the reinforcing effects of pleasurable stimuli, including the effects of drugs[24].

Not many studies have correlated the neurological, neuropsychological and personality factors that may have a predictive role in relapse management of alcohol use disorder patients. This study was planned to make-up for the dearth of such studies and particularly so in Indian population.

Aim

To study the personality and neurobiological factors associated with relapse in alcohol dependent patients.

Methodology

This was a cross-sectional study carried out at deaddiction ward of the Department of Psychiatry, SMS Medical College, Jaipur. 60 consecutive patients of alcohol dependence admitted for detoxification and management were recruited for the study, after fulfilling pre-

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defined inclusion and exclusion criteria and written informed consent was taken from them before subjecting to tools of study.

Inclusion criteria

1. Patients who met the ICD-10 criteria for Mental and behavioral disorder due to alcohol dependence, currently abstinent in controlled environment, who had completed their pharmacological detoxification.
2. Age 18–60 years, either sex.
3. Literate enough to understand and perform the questionnaires.
4. Willing to give written consent and participate in the study.

Exclusion criteria

1. A severe disorder either in terms of behavior, communication or language that will make the interview almost impossible.
2. Patients undergoing treatment of alcohol dependence for the first time and/or lacking a history of abstinence.
3. History of significant anyother substance abuse, in last 6 months, except nicotine. (ICD-10)
4. History of electroconvulsive therapy in the previous six months.
5. History of neurological disorder/ significant head injury.
6. Mental retardation/ Pregnancy/ Breast feeding
7. Any h/o chronic medical illness

Tools of study

1. SOCIODEMOGRAPHIC PROFILE: This semistructured performa will include name, age, sex, father's /husband's name, address, marital status, education, occupation, type of family and monthly income.
2. CLINICAL PROFILE PERFORMA: This self-designed performa will include detailed history of alcohol dependence, age at onset, type of last detoxification, duration of abstinence, current treatment status and details of treatment taken.
3. SEVERITY OF ALCOHOL DEPENDENCE QUESTIONNAIRE[25]: It is a subjective scale consisting of 20 questions related to alcohol dependence, rated on a likert scale of 0-3. Total SADQ score is analysed as: a score 0-3- no dependence, 4-19- mild dependence, 20-30- moderate dependence, 31-44+- severe dependence, 45+- very severe dependence.
4. EYSENCK PERSONALITY INVENTORY- REVISED SHORT FORM (HINDI)[26]: It is a 48-item clinician rated scale that measures personality traits on 3 dimensions- Neuroticism, Psychoticism, Extraversion and Lie (control subscale). A validated hindi version of this scale in available for application in Indian patients.
5. OBSESSIVE COMPULSIVE DRINKING SCALE (OCDS)[27]: The Obsessive Compulsive Drinking Scale (OCDS) is the most widely used alcohol craving instrument. The OCDS has been validated in adults with Alcohol Use Disorders (AUDs). Scores on each

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item can range from 0-4, with higher scores indicating higher obsessions and compulsions with alcohol. The total score range is from 0-40. An OCDS total score of 7 and above discriminates between social drinkers and alcohol dependent drinkers, with a sensitivity of 93% and a specificity of 98%.

6. HAMILTON RATING SCALE FOR DEPRESSION (HAM-D)[28]:It is the most widely used clinician administered depression assessment scale. It contains 17 items pertaining to symptoms of depression experienced over the past week and is used to assess the severity of depressive symptoms. It takes 20-30 mins to administer. A score < or = 7 is considered normal, 7 - 13 (mild depression), 14 - 24 (moderate to severe depression), > 24 (severe depression).
7. HAMILTON RATING SCALE FOR ANXIETY (HAM-A)[29]:It is a clinician rated anxiety scale that measures the degree of person's pathological anxiety condition. It consists of 14 items which are related to anxiousness, tension, fears, insomnia, intellectual (cognitive), depressed mood, somatic (muscular), somatic (sensory) cardiovascular, respiratory, gastrointestinal, genitourinary and autonomic symptoms. Each item is rated as 0 to 4 and scores of all items are summed up to give total score of anxiety, classified as 14-17 = Mild Anxiety, 18-24 = Moderate Anxiety and 25-30 = severe Anxiety.
8. NEUROPSYCHOLOGICAL BATTERY:We gave the patients six tests which are described below in the same order in which they were presented to the subjects[30-35]
    a. Digit span test (Weschler,1981)
    b. Verbal learning and memory test (Mukundan, 1991)
    c. Visual learning and memory test (Mukundan, 1991)
    d. Visuo-spatial working memory matrix (Vecchi, 1995)
    e. Stroopcolour test (Stroop, 1935)
    f. Trail making Test A & B (Reiten, 1958)
9. CAMBRIDGE NEUROLOGICAL INVENTORY (CNI)[36]: The CNI is a brief standardized clinical instrument specifically devised and validated for its use with psychiatric, rather than neurological patients. Part 2 of the inventory is for Soft sign examinations. Ratings on the CNI are standardised to indicate 'normal response' (0), 'equivocal response' (0.5), 'abnormal response' (1) or 'grossly abnormal response' (2).

Statistical analysis

Descriptive data was analysed in frequencies, percentages, mean and standard deviations. Comparisons among groups was established using chi-square testsand independent T- tests. The results were considered significant at $p<0.05$. All tests were applied using the software, SPSS, ver. 21, IBM Corp.

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Results

Taking a period of 6 months as the period of active intervention, the data was analysed by dividing the patients into two groups: those who abstained for less than 6 months and those who abstained for more than 6 months[37].

The two groups of patients did not differ significantly on sociodemographic parameters like age, sex, religion, education level, occupation, residence and socioeconomic status. [TABLE-1]

The mean age of onset of alcohol consumption was significantly lower in those who relapsed in less than 6 months (t=-3.362, p=0.001). The two groups also differed significantly in the presence of family history (t=21.600, p=0.000), severity of alcohol dependence (t=40.000, p=0.000) and the type of previous detoxification (t=19.288, p=0.000). [TABLE-2]

The two groups differed significantly from each other on the parameters of comorbid depression (t=2.250, p=0.028), anxiety (t=3.152, p=0.003), obsessive compulsive drinking score (t=19.223, p=0.000) and psychoticism (t=7.212, p=0.000). [TABLE-3]

Upon administration of neuropsychological tests, the two groups of patients differed significantly from each other in performance of verbal learning and memory test (t=-7.884, p=0.000), visuospatial working memory matrix (t=-6.528, p=0.000) and trail making A (t=5.221, p=0.000) and B (t=21.104, p=0.000) tests. [TABLE-4]

When tested for neurological soft signs, the two groups differed significantly from each other in the domains of motor coordination (t=10.681, p=0.000) and disinhibiton (t=6.843, p=0.000). [TABLE-5]

TABLE-1: SOCIODEMOGRAPHIC PROFILE

SOCIODEMOGRAPHIC FACTORS		Duration of Abstinence <6months	Duration of Abstinence >6months	X^2 (d.f.)*	SIGNIFICANCE LEVEL (2-sided)£
AGE	</= 35 YEARS	12	9	4.038(1)	0.133
	>35 YEARS	18	21		
SEX	MALE	30	30	-	-
RELIGION	HINDU	26	22	1.667(1)	0.197
	MUSLIM	4	8		
EDUCATIONAL LEVEL	MIDDLE SCHOOL	15	13	3.534 (3)	0.316
	SECONDARY	13	10		
	SENIOR SECONDARY	1	2		
	GRADUATE AND HIGHER	1	5		

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OCCUPATION	UNSKILLED	25	22	2.191 (3)	0.534
	SEMISKILLED	2	4		
	SKILLED/ PROFESSIONAL	1	3		
	UNEMPLOYED	2	1		
RESIDENCE	URBAN	15	19	1.086 (1)	0.297
	RURAL	15	11		
SOCIOECONOMIC STATUS	LOWER	25	24	1.163 (2)	0.559
	MIDDLE	4	3		
	UPPER	1	3		

*Chi-square test, d.f.-degrees of freedom, £Significance level at <0.05

TABLE-2: CLINICAL PROFILE

CLINICAL PROFILE	DURATION OF ABSTINENCE	Mean	Std. Deviation	t-Value (d.f.)*	Sig. (2-tailed)£
AGE AT ONSET (in years)	<6 months	19.567	2.0457	-3.362 (58)	**0.001**
	>6 months	22.033	3.4590		

*Independent t-test, d.f.-degrees of freedom, £Significance level at <0.05

CLINICAL PROFILE		DURATION OF ABSTINENCE		X^2 (d.f.)*	Signi. (2-sided)£
		<6 months	>6 months		
FAMILY HISTORY	Absent	6	24	21.600 (1)	**0.000**
	Present	24	6		
SEVERITY OF ALCOHOL DEPENDENCE (SADQ SCORES)	Mild	0	20	40.000 (3)	**0.000**
	Moderate	10	10		
	Severe	16	0		
	Very severe	4	0		
TYPE OF PREVIOUS DETOXIFICATION	OPD	6	23	19.288 (1)	**0.000**
	IPD	24	7		

*Chi-square test, d.f.-degrees of freedom, £Significance level at <0.05

TABLE-3: PERSONALITY FACTORS

PERSONALITY FACTORS	DURATIONOF ABSTINENCE	Mean	Std. Deviation	t-Value (d.f.)*	Signi. (2-tailed)£
COMORBID DEPRESSION	<6 months	9.133	4.6663	2.250 (58)	**0.028**
	>6 months	6.967	2.4563		
COMORBID ANXIETY	<6 months	15.400	5.8933	3.152 (58)	**0.003**
	>6 months	11.333	3.8981		
OBSESSIVE COMPULSIVE DRINKING SCORE	<6 months	27.033	4.8101	19.223 (58)	**0.000**
	>6 months	7.967	2.5255		
EXTRAVERSION	<6 months	8.167	1.6206	-4.104 (58)	**0.000**
	>6 months	9.633	1.0981		
NEUROTICISM	<6 months	7.433	.9353	1.247 (58)	0.217
	>6 months	7.067	1.3113		
PSYCHOTICISM	<6 months	7.833	1.8210	7.212 (58)	**0.000**
	>6 months	5.033	1.0981		

*Independent t-test, d.f.-degrees of freedom, £Significance level at <0.05

TABLE-4: NEUROPSYCHOLOGICAL BATTERY

Neuropsychological tests	DURATION OF ABSTINENCE	Mean	Std. Deviation	t-Value (d.f.)*	Signi. (2-tailed)£
DIGIT SPAN	<6 months	12.433	1.3309	-1.246 (58)	.218
	>6 months	12.900	1.5614		
VERBAL LEARNING AND MEMORY TEST	<6 months	69.867	6.9468	-7.884 (58)	**.000**
	>6 months	84.500	7.4220		
VISUAL LEARNING AND MEMORY TEST	<6 months	66.133	6.8969	-1.653	.104
	>6 months	68.633	4.5900		
VISUO-SPATIAL WORKING MEMORY MATRIX	<6 months	4.533	1.1059	-6.528 (58)0	**.000**
	>6 months	6.267	.9444		
STROOP TEST (TIME IN SECONDS)	<6 months	133.767	7.2430	1.718 (58)	.091
	>6 months	130.967	5.2159		
STROOP TEST (NO. OF ERRORS)	<6 months	24.800	2.7089	1.667 (58)	.101
	>6 months	23.333	3.9856		

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TRAIL MAKING TEST- A	<6 months	51.833	3.8603	5.221	**.000**
	>6 months	45.267	5.7050	(58)	
TRAIL MAKING TEST- B	<6 months	133.033	6.0371	21.104	**.000**
	>6 months	94.767	7.8858	(58)	

*Independent t-test, d.f.-degrees of freedom, £Significance level at <0.05

TABLE-5: NEUROLOGICAL SOFT SIGNS

NEUROLOGICAL SOFT SIGNS	DURATION OF ABSTINENCE	Mean	Std. Deviation	t-Value (d.f.)*	Signi. (2-tailed)£
MOTOR COORDINATION	<6 months	7.400	1.1017	10.681	**0.000**
	>6 months	4.533	.9732	(58)	
SENSORY INTEGRATION	<6 months	5.167	.9129	1.984	0.052
	>6 months	4.333	.9942	(58)	
DISINHIBITION	<6 months	2.233	.9353	6.843	**0.000**
	>6 months	.800	.6644	(58)	

*Independent t-test, d.f.-degrees of freedom, £Significance level at <0.05

Discussion

This study was planned to identify personality factors, neurological and neurocognitive indicators which may be predictors of early relapse in patients of alcohol dependence. The patients were divided into two groups for analysis- one of those who relapsed within first 6 months of last attempt of detoxification, i.e. within the active intervention phase and second group of those who relapsed after 6 months[37]. Also, patients were recruited after completion of their pharmacological detoxification to avoid any influence of drugs and active withdrawal symptoms on the performance of neurocognitive tests and neurological soft signs.

The two groups did not differ from each other on sociodemographic characteristics like age, sex, religion, educational status, occupational status, residence locality and socioeconomic status. Influence of these factors on relapse was not found. Although there are studies which predict better outcomes and longer abstinence periods with sociodemographic factors like being employed[38], having familysupport[39-42], female gender[38], older age[38]and more years of schooling[43], our study did not find any such difference. The likely reason for this finding is that this study was confined to admitted patients of alcohol dependence, the sociodemographic profile of the patients availing treatment in government setup group may have got restricted. Also, we did not find any female inpatients which can be attributed to lesser incidence and conservative attitude of society towards alcohol use disorders in females, leading to a possible skew.

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The mean age of onset of alcohol consumption was significantly lower in those who relapsed in less than 6 months (t=-3.362, p=0.001). The average age of onset in patients who abstained for less than 6 months was 19.57+/-2.0457 years and that of patients who abstained for longer than 6 months was older (22.033+/-3.4590 years). This meant that those who started consuming alcohol at an earlier age and had longer duration of illness were more likely to relapse within the active intervention phase of 6 months. Many studies also quote similar findings that a younger age at the onset of alcoholdependence[44], more lifetime drinking problems[44] and more previous treatments[45,46] were correlated to earlier relapses. The two groups also differed significantly in the presence of family history (t=21.600, p=0.000). Family history was more likely to be present in patients who relapsed earlier than those who relapsed later than 6 months. Presence of family history is a significant contributor to the course of alcohol dependence since it signifies an earlier and frequent exposure to alcohol use and often there is social agreement and easy availability in such families, facilitating frequent and earlier relapses. This finding is also shown by many studies predicting treatment outcomes in alcohol dependent patients[45,46].

Severity of alcohol dependence (t=40.000, p=0.000) was more severe in the group that abstained for less than 6 months than those who abstained for longer than 6 months. These patients who relapsed earlier also had a history of previous inpatient detoxification (t=19.288, p=0.000). Inpatient detoxification is usually needed for patients with moderate to severe alcohol dependence or those who have experienced a complicated withdrawal prior, and hence is an indicator of a history of more severe form of alcohol use disorder and hence earlier relapse. This finding is contradicted by a study which claims better outcomes in patients treated as inpatients or for longer durations[47-49].Patients who have a more severe dependence of alcohol often have severe withdrawals and have a lower urge and motivation to quit alcohol, which leads to poorer outcomes of treatment and relapses[38,39,50].

The two groups differed significantly from each other on the parameters of various personality factors and comorbid conditions. Comorbid depression (t=2.250, p=0.028) and anxiety (t=3.152, p=0.003) were more likely in patients who abstained for less than 6 months.Obsessive compulsive drinking score was also higher in these patients (t=19.223, p=0.000) and is a significant predictor of relapse in early intervention period of 6 months[37,51]. Patients who experience depression, anxiety and compulsiveness often engage in alcohol use for self medication and relief of symptoms[52]. These patients also exhibit poorer coping skills[53], lack of self efficacy[53] and hence a higher likelihood to relapse, even before the active intervention phase of 6 months has lapsed[51,53,54]. Earlier and more frequent relapses have been known to be correlated with high psychoticism[23,55], as has been shown in our study as well. (t=7.212, p=0.000). High psychoticism is a marker for increased impulsiveness in patients of alcohol dependence leading to earlier and frequent relapses[55].

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Upon administration of neuropsychological tests, the two groups of patients differed significantly from each other in performance of verbal learning and memory test (t=-7.884, p=0.000), visuospatial working memory matrix (t=-6.528, p=0.000) and trail making A (t=5.221, p=0.000) and B (t=21.104, p=0.000) tests. The patients who abstained for less than 6 months performed worse than those who abstained from alcohol for more than 6 months.When tested for neurological soft signs, the two groups differed significantly from each other in the domains of motor coordination (t=10.681, p=0.000) and disinhibiton (t=6.843, p=0.000). The patients who had earlier relapse performed worse than the ones who abstained for longer than 6 months. The fact that alcoholics showobservable deficits in cognition has long beenrecognized[56]. Similar findings have been demonstrated in previous studies where a worse performance of neuropsychological battery and exhibition of neurological soft signs correlated with frequent and earlier relapses and poorer outcomes[57]. Although an improvement in neuropsychological functioning has been documented after *5* years ofabstinence[58], it has been shown that alcoholicsare most severely impaired during the first week of abstinence, and that their performance returns to normal thereafter[59,60].

Conclusion

These findings pave way for a larger study with a wider patient selection, inclusive of both inpatients and outpatients to improve the generalizability and reliability of these findings. Nevertheless, the uniqueness of this study lies in the fact that it is one of the few studies done on Indian patients of substance use disorders, where personality and neurocognitive dimensions have been studied in an attempt to elucidate factors related to relapse in patients of alcohol dependence. These factors were selected keeping in mind their predictive value and their implication in long-term management of these patients.

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