

Assessment of Platelets Monoamine Oxidase-B (MAO-B) Activity Levels and Cognitive Functions in Patients of Alcohol Dependence and Healthy Controls: A Comparative Study

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Abstract

Objectives: Study was to assess platelet Monoamine Oxidase-B (MAO-B) activity levels and cognitive functions in alcohol-dependent patients and healthy controls. A possible correlation between platelet MAO-B levels and cognitive functions was also explored.

Methods: 22 alcohol-dependent patients and healthy controls were recruited, and platelet MAO-B levels and cognitive functions were assessed by different laboratory and psychological tests respectively.

Results: Findings revealed lower levels of platelet MAO-B levels and poor cognitive functions in alcohol-dependent patients as compared to controls. Platelet MAO-B activity was significantly associated with only visual retention domain of cognitive functions.

Conclusions: Findings revealed low platelet MAO-B levels and poor cognitive performance in alcohol dependents. Thus, more prospective studies can make us more hopeful to use MAO-B levels as a potential biomarker for alcohol consumption, early abstinence or detoxification, and cognitive functions.

Keywords: Platelets MAO-B Activity, Cognitive Function, Alcohol Dependence, Nicotine Dependence

Introduction

Alcohol dependence is a public health problem. Alcohol apart from having direct toxic effect on body, also impairs cognition, affect, and behavior. It's estimated that 50-80% of alcohol dependents experience mild to severe neurocognitive impairment of different domains that remain impaired even during short- and long-term abstinence in many patients [1]. However, there are inconsistencies about the domains and their severity of impairment.

In alcohol-dependence, low platelet Monoamine Oxidase-B (MAO-B) activity has been proposed as a possible biochemical marker [2]. Literature suggests that MAO-B activity remains low in alcohol-dependent patients compared to healthy individuals during active alcohol consumption, during active withdrawal and after abstinence period [2, 3]. But there are studies where no difference could be established among alcoholics and control subjects. As there are multiple confounding factors which can also alter the MAO activity levels [4]. Furthermore, alcohol-dependent patients show significant associations between low

platelet MAO-B activity, and impairment in cognitive domains such as reaction time, maze checking time, motor disinhibition task, executive functions, nonverbal reasoning [2]. The findings of existing literature are variable, and till now no such associations have been explored in the Indian population.

Considering mentioned inconsistencies and gap in literature, with limited recent studies, the aim of present study was to assess platelet MAO-B activity level and cognitive functions of alcohol-dependent patients and further explore correlation between platelet MAO-B activity level and cognitive functions. To the best of our knowledge, this is the first Indian study to explore such associations.

Participants and Methodology

Setting and Participants

It was a cross-sectional study, completed in 4-months' duration at Outpatient Department of tertiary care center in India. Study included first time visiting 22 male patients between the age group of 18 to 60 years, fulfilling criteria for alcohol dependence

syndrome as per ICD-10. Similarly, 22 control participants recruited from friends of patients who were illness-free except tobacco use. At recruitment patients who were intoxicated, having significant withdrawals (Clinical Institute Withdrawal Assessment of Alcohol Scale, revised, CIWA-Ar score ≥ 9) had known co-morbid psychiatric illness, benzodiazepines use in past week, severe medical illnesses or clinically sub-normal intelligence were excluded from the study. The study was approved by the Institute Ethics Committee, and written informed consent was taken from each participant.

The severity of alcohol dependence was assessed by using the Severity of Alcohol Dependence Questionnaire (SADQ) [5]. To assess the socioeconomic status of participants, Modified Kuppuswamy's scale was applied; Mini-International Neuropsychiatric Interview (MINI) was applied to assess the common psychiatric disorders among patients and controls; Clinical Institute Withdrawal Assessment of Alcohol Scale, revised (CIWA-Ar) was applied to assess the severity of alcohol withdrawal; Fagerstrom Test for Nicotine Dependence (FTND) smoking and smokeless form were applied for assessment of severity of nicotine dependence [6-9].

Neurocognitive functions were assessed in the first week of abstinent from alcohol, those participants who were having significant withdrawals on CIWA-R scale excluded from the study. Cognitive functions were assessed using different scales, Wechsler Adult Intelligence Scale-Fourth Edition (INDIA) (WAIS-IVINDIA) used to assess Working Memory Index and Processing Speed Index, Category Fluency was done to evaluate executive functions and language, Stroop Test was applied to

assess cognitive flexibility and resistance to interference from outside stimuli (NIMHANS-version), Trail Making Test (TMT) used for assessment of visual search, scanning, speed of processing, mental flexibility, and executive functions, memory functions were assessed using P.G.I. Memory scale, Urine rapid cassette test was done to screen opioids, benzodiazepines, and cannabis use [10-14].

Determination of Blood Platelets MAO-B Activity

From each participant, 5ml of random blood was collected during first week of abstinent from alcohol. It was centrifuged at 1000 rpm for 10 minutes on 4°C of temperature to obtain platelet-rich plasma (PRP). This PRP was kept at -70°C for estimating MAO-B activity by ELISA.

Statistical Analysis

Study analysis was carried out by using SPSS version 21. The demographic profile and qualitative data of two groups were compared using descriptive statistics and chi-square respectively. Study data was checked for normal distribution. A comparison between MAO-B levels and psychological test performances was done by using student t-test. Correlation between platelets MAO-B activity and cognitive function scores were evaluated by using Pearson's correlation coefficient. For all comparisons $p < 0.05$ was considered significant.

Result

Socio-Demographic Profile

On independent sample t-test, statistically, no significant difference was observed in age, educational qualifications, and socio-economic status of both groups (Table:1).

Table 1: Socio-demographic profile of the patients

Variables	Patients (N=22)	Control group (N=22)	Comparison (Statistic, p-value)
	N (%)	N (%)	Independent sample t-test/Chi-square test
Age(years) Mean (S.D)	34.77 (6.82)	33.27 (7.89)	t= 0.674, p= 0.50
Marital status			
Never married	02(09.1)	07 (31.8)	$\chi^2= 3.492$, p= 0.06
Ever married	20(90.9)	15 (68.2)	
Education			
High school	08 (36.4)	08 (36.4)	$\chi^2= 0.583$, p= 0.74
Intermediate	05 (22.7)	07 (31.8)	
Graduate/Postgraduate	09 (40.9)	07 (31.8)	
Occupation			
Unemployed/Unskilled	07 (31.8)	01 (04.5)	$\chi^2= 7.858$, p= 0.04*
Semiskilled/skilled	04 (18.2)	11 (50.0)	
Clerical/shopkeeper	06 (27.3)	05 (22.7)	
Prof./Semi-professional	05 (22.7)	05 (22.7)	
Family type			
Nuclear	08 (36.4)	08 (36.4)	$\chi^2= 0.09$, p= 0.75
Extended	14 (63.6)	14 (63.6)	
Residential area			
Urban	18 (81.8)	16 (72.7)	$\chi^2= 0.518$, p= 0.47
Rural	04 (18.2)	06 (27.3)	

Family income monthly (INR)			
< 13494	12 (54.5)	09 (40.9)	$\chi^2= 2.752, p= 0.25$
13495- 36016	04 (18.2)	09 (40.9)	
> 36016	06 (27.3)	04 (18.2)	
Religion			
Hindu	20 (90.9%)	22 (100%)	$\chi^2= 2.095, p= 0.14$
Muslim	02 (09.1%)	00 (00%)	
Socio-economic status (SES)			
Upper-Lower SES	04(18.2)	01 (04.5)	$\chi^2= 2.053, p= 0.35$
Lower-Middle SES	09(40.9)	11 (50.0)	
Upper-Middle/Upper SES	09(40.9)	10 (45.5)	

(*p < 0.05, **p< 0.01)

Clinical Profile

All included patients fulfilled the criteria of alcohol dependence and nicotine dependence. Most of them were not on treatment for alcohol dependence. The mean age of starting alcohol use was 24.68 years (SD 5.34). On SADQ, 15(68.2%) patients had moderate alcohol dependence and 7(31.8%) had severe alcohol dependence. All the participants who were using tobacco were taking it in a dependent pattern. Among recruited patients, 16(72.7%) were taking tobacco in smoking form and 6(27.3%) were taking as smokeless form. In the control group, 14(63.6%) participants were using tobacco in smoking form and 8(36.4%) were using smokeless form. Both groups were comparable in smoking form of tobacco use.

Cognitive Functions

On TMT A and B, patients took significantly more time to complete tests compared to controls ($p < 0.001$). On intelligence scale patients scored significantly low on working memory index (WMI) and processing speed index (PSI) compared to healthy controls ($p < 0.001$), on color Stroop test, patients performed significantly poorer than controls ($p = 0.04$). On PGI memory scale, in most domains (remote memory, mental balance, attention and concentration, immediate recall, and mean of the total score) patients scored significantly poorer compared to control ($p < 0.05$). No statistically significant differences were found on category fluency score, Stroop word score, and Stroop effect (Table-2).

Table 2: Scores of different domains on Neurocognitive Tests

Test	Mean (SD)		Independent sample t-test (Statistic, p-value)
	Patients (N=22)	Control group (N=22)	
Trail Making Test (TMT)			
TMT Part A	39.54 (4.29)	33.77 (4.82)	t= 4.1891, p< 0.001**
TMT Part B	124.09(27.16)	91.36(14.65)	t = 4.973, p<0.001**
Category fluency test			
No. of words per minute	11.27 (1.75)	12.13(1.52)	t= 1.746, p= 0.08
Wechsler Adult Intelligence Scale (WAIS)			
Working memory index	66.45 (5.38)	75.00 (4.98)	t= -5.460, p< 0.001**
Processing speed index	67.40 (5.90)	74.45 (6.41)	t= -3.789, p<0.001**
Digit forward	06.63(0.90)	07.36(0.72)	t= -2.944, p= 0.005**
Digit backward	05.72(1.07)	06.45(0.85)	t= -2.477, p= 0.01*
Digit span	04.50(0.74)	05.36(0.72)	t= -3.90, p<0.001**
Arithmetic	10.22(1.41)	12.22(1.37)	t= -4.755, p<0.001**
WAIS Symbol	16.31(4.19)	23.27(3.90)	t= -5.694, p< 0.001**
WAIS Coding	34.95(6.30)	35.86(6.19)	t= -0.482, p= 0.63
Stroop Test			
Word score	97.04(20.68)	87.04(13.68)	t= 1.891, p= 0.06
Colour score	153.40(35.40)	135.13(22.51)	t= 2.042, p= 0.04*
Stroop effect	56.36 (28.58)	48.09 (16.71)	t= 1.172, p= 0.24
P.G.I. Memory scale			
Remote memory	0.46 (0.15)	0.37 (0.09)	t= 2.295, p=0.02*
Recent memory	-0.86 (1.62)	-0.25 (1.25)	t= -1.378, p=0.17

Mental balance	-0.28 (0.81)	0.15 (0.56)	t= -2.092, p=0.04*
Attention & concentration	-1.05 (0.70)	-0.63 (0.61)	t= -2.090, p=0.04*
Delayed recall	-0.19 (0.91)	0.26 (0.68)	t= -1.881, p=0.06
Immediate recall	1.20 (0.80)	1.68 (0.27)	t= -2.675, p=0.01*
Retention for similar pairs	-0.04 (0.96)	0.13 (0.78)	t= -0.687, p=0.49
Retention for dissimilar pairs	-0.02 (0.42)	-0.01 (0.76)	t= -0.033, p=0.97
Visual retention	-0.07 (0.95)	-0.07 (0.78)	t= 0.027, p=0.98
Recognition	-0.79 (1.02)	-0.44 (0.92)	t= -1.210, p=0.23
Total score	-0.21 (0.74)	0.28 (0.61)	t= -2.394, p= 0.02*
Platelets MAO-B activity level			
MAO-B (nmol/mg protein/hour)	4.36 (0.88)	4.98 (0.91)	t= -2.303, p= 0.02*

(*p ≤ 0.05, **p ≤ 0.01)

Platelet MAO-B Activity

Platelet MAO-B activity was significantly lower in alcohol-dependent patients than healthy controls (p=0.02) (Table-2). It showed a significant correlation with only visual retention domain (p= 0.04).

Discussion

Findings of present study support the hypothesis of lower platelet MAO-B activity in alcohol-dependence, these findings are also in line with Indian study done by Rajesh et al in 2010 [15-17]. Previous studies had also reported low platelet MAO-B activity, during active withdrawal after abstinence from alcohol and after a certain abstinence period [2, 3, 15]. In present study MAO-B activity was measured during early abstinence period (1st-week), but due to cross-sectional design of study, we cannot infer whether low platelet MAO-B activity is a trait/state marker of alcohol use or current abstinence. Low platelet MAO-B activity in alcohol dependence maybe because of inhibiting effect of ethanol on MAO-B [15].

Platelet MAO-B activity can be influenced by multiple factors e.g. smoking, age, sex, genetics, personality traits, and environment [15]. The effect of smoking on platelet MAO-B activity has been variable from inhibitory effect to nil effect [15, 18]. The present study nullified the effect of smoking by recruiting matched controls. Reporting of low MAO-B activity solely due to smoking in previous studies is contradictory to our study's findings. Moreover, smokeless tobacco does not alter platelet MAO-B level [18]. Previous studies reported lower platelet MAO-B activity in males than females and an increase in platelet MAO-B activity with aging to overcome these confounders present study recruited only male participants with comparable age group [16, 19].

Patients performed significantly poorer than controls on different psychological tests e.g., visual search speed, scanning, speed of processing, mental flexibility and executive functioning as assessed by TMT A and B. Patients had significantly worse working memory and processing speed than controls. Similarly, patients had significantly poorer remote memory, mental balance, attention & concentration, and immediate recall. This study replicated the findings of previous studies where alcohol-dependent patients performed significantly worse than controls on different cognitive tasks [20].

Cognitive impairments in alcohol-dependence may be due to involvement of frontal lobe, which supports frontal lobe hypothesis of alcoholism [19]. Cognitive functions were assessed only in early abstinence period so due to the cross-sectional design of study course of cognitive deficits cannot be explained. Our study was not able to ascertain whether cognitive deficits precede alcohol or vice versa. Thus, it recommends, bigger prospective study to explore how cognitive functioning varies during abstinence periods.

Study findings showed significant correlation between low platelet MAO-B activity and visual retention domain of cognitive functions. In contrast, previous studies had shown significant association of low MAO-B activity with various cognitive domains such as response time, failed inhibition, and maze perceptual check time [3, 21]. Another study by Demir et al., 2002 showed no such associations [2]. Our study was not able to replicate similar domains as of previous studies, may be because of limited sample size.

Conclusion

The present study highlighted low Platelet MAO-B activity and poor cognitive performance in alcohol-dependent patients. Study shown only significant correlation between MAO-B levels and visual retention domain of cognitive function. With evidence from previous studies, serial monitoring of MAO-B activity can be a good guide for determining dependence, early abstinence, or detoxification in alcohol-dependence. Thus, platelet MAO-B levels with more robust evidence may come up as a potential biomarker in alcohol dependence. New advancements in our understanding of MAOs and its implication in alcohol dependence will be fruitful for future research directions and clinical outcomes. Findings of present study also necessitate a prospective study with large sample size to explore how MAO-B levels and cognitive functions fluctuate during abstinent and their correlation in alcohol-dependence.

Limitations

Limited sample size reduces the power and validity of study. Secondly, effect of other confounders like personality traits, type of dependence, genetic factors, protein metabolism, hormonal, and environmental factors have not been taken into consideration which may influence the findings. Also, cross-sectional design of study cannot guide us that how platelet MAO-B level and cognitive functions fluctuate during long-term abstinence.

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Declaration of Conflict of Interest

We declare no conflicts of interest.

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Presentation at the Meeting

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