ORIGINAL ARTICLE

ASIAN JOURNAL OF MEDICAL SCIENCES

A study of cognitive impairment and its neuroimaging correlates in patients with alcohol dependence a cross-sectional study

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Submission: 04-04-2023 Revision: 28-08-2023 Publication: 01-10-2023

ABSTRACT

Background: Alcohol abuse is one of the most common psychiatric disorders observed worldwide. **Aims and Objectives:** The study aimed to assess cognitive impairment in alcohol-dependent patients, its correlation with neuroimaging, and compare the findings with non-alcoholics. **Materials and Methods:** We have included 30 alcoholics and 30 control participants. Tools such as semi-structured pro forma, alcohol use disorder identification test score, the severity of alcohol dependence questionnaire (SADQ), and PGI memory scale (PGIMS) were used for the assessment. The measurements of the third and fourth ventricle width, interhemispheric fissure width, cerebellar transverse width, the inner diameter of the skull, anterior horn distance, and midbrain diameter were taken from a magnetic resonance imaging (MRI) brain. **Results:** There was a significant difference in remote memory, mental balance, attention and concentration, delayed recall, immediate recall, visual retention, third and fourth ventricle width, interhemispheric fissure width, and cerebral transverse length between alcoholics and non-alcoholics. Further, a correlation analysis of the PGIMS total score with MRI measurements and alcohol intake showed a significant negative correlation of PGIMS total score with third ventricle width, duration of alcohol consumption, period of alcohol dependence, the quantity of alcohol per day, and SADQ score. However, a significantly positive correlation was observed between PGIMS total score and cerebellar transverse length. **Conclusion:** Alcohol-dependent patients had poor cognitive functions compared to non-alcoholics. They also had significant cerebral and cerebellar atrophy and were characterized by dilation of the third and fourth ventricles. The increase in the duration of alcohol consumption, period of alcohol dependence, and quantity of alcohol intake caused cognitive impairment independently.

Key words: Alcohol dependence; Cognitive impairment; Alcohol use disorder identification test; Severity of alcohol dependence questionnaire; PGI memory scale

Access this article online

Website:

http://nepjol.info/index.php/AJMS

DOI: 10.3126/ajms.v14i10.53860

E-ISSN: 2091-0576

P-ISSN: 2467-9100

INTRODUCTION

Alcohol abuse is one of the most common psychiatric disorders observed worldwide. It is a powerful drug that causes acute and chronic alterations in the neurochemical system. Alcohol abuse can cause significant psychological symptoms such as anxiety, neurosis, and depression.[1] According to the Global Health Observatory Data (2018), harmful alcohol use results in the death of 3 million people annually. This represents nearly 1 in 20 total deaths. More than 3 quarters of alcohol-related deaths were among men. In 2016, worldwide total alcohol consumption was equal to nearly 6.4 L of pure alcohol per person 15 years and older. Unrecorded consumption amounts to 26% of worldwide total alcohol consumption.[2]

Chronic alcohol use has been associated with numerous cognitive deficits such as executive dysfunction, poor working memory, verbal fluency impairment, spatial processing problems, and response inhibition.[3] Studies

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stated that such cognitive impairments can be attributable to structural brain changes observed in magnetic resonance imaging (MRI).[4,5] Thus, the present study aimed to evaluate the cognitive impairment and its neuroimaging correlation in patients with alcohol dependence and to compare the findings with non-alcoholics.

Aims

To study the cognitive impairment and its neuroimaging correlates in patients with alcohol dependence.

Objectives

- To assess the cognitive impairment in patients with alcoholdependence.
- To study the neuroimaging changes in patients with alcohol dependence.
- To determine the correlation between cognitive impairment and neuroimaging changes.

MATERIALS AND METHODS

It was an observational cross-sectional study conducted at Tirunelveli Medical College, Tirunelveli, a tertiary care center in Tamil Nadu, from January 2018 to April 2019. The study has received approval from Institutional Ethical Committee, Tirunelveli Medical College, Tirunelveli. We have included 60 patients (30 cases and 30 controls).

Inclusion criteria

Male patients aged between 20 and 50 years, patients who are admitted to the de-addiction ward, who fulfill the International Statistical Classification of Diseases and related health problems (ICD)-10 criteria for alcohol dependence, non-alcoholic male patients underwent MRI brain screening for non-seriously ill medical or neurological conditions such as chronic headache, migraine, giddiness, and vertigo.

Exclusion criteria

Males aged <20 years and more than 50 years and females, patients with major mental illness and severe physical comorbidities, patients on any psychotropic medications except benzodiazepines, anti-craving drugs, and disulfiram, individuals with a history of head injury, pre-existing neurological illness, and history of substance abuse were excluded from the study.

The interview and assessment were conducted in the hospital during the patient's admission and in review clinics in a single sitting. Patients were interviewed using semi-structured pro forma. All the instruments were used after the patient was detoxified and became amenable to administering rating scales. The alcohol dependence was assessed using the alcohol use disorder identification test (AUDIT) score. The severity of alcohol dependence was assessed using the severity of alcohol dependence questionnaire (SADQ). The presence of cognitive impairment was tested using the PGI memory scale (PGIMS).

MRI brain was performed with Siemens Magnetom Amira 1.5 tesla machine in Tirunelveli Medical College. No sedation was administered to the patient for an MRI examination. A standard protocol was used for MR brain image acquisition. The section thickness was 5 mm. The images were analyzed, and the measurements for the third and fourth ventricle width, interhemispheric fissure width, transverse cerebellar length, the inner diameter of the skull, anterior horn distance, and midbrain diameter were done.

Statistical analysis

Cognitive functions and MRI imaging measurements were assessed. The Chi-square test was used to compare the sociodemographic details between the study and the control groups. Student *t*-test was applied to compare the mean values between the groups for cognitive functions and MRI measurements. The Pearson correlation coefficient was used to find the correlation between cognitive functions and MRI measurements. Kendall's tau-b correlation coefficient was used to find any correlation between alcohol intake and PGIMS total score. $P<0.05$ was considered as statistically significant.

RESULTS

The sociodemographic details of the study participants are shown in Table 1. The total number of cases and controls included in our study was 30 in each group. The mean age of the case and control was 39.6 and 34.2 years, respectively. Most subjects fall in the age category of 40–50 years. We have seen a significant difference in the marital status of the case and control groups (Table 1).

A comparison of cognitive function in study groups indicated a significant difference in cognitive functions, including remote memory, mental balance, attention and concentration, delayed recall, immediate recall, visual retention, and total PGIMS score (Table 2).

Further, comparing MRI measurements between case and control groups indicated a significant difference in MRI measurements, including third ventricle width, fourth ventricle width, and interhemispheric fissure width (Table 3).

In addition, we have performed a correlation analysis of the PGIMS total score (cognitive functions) with MRI measurements and alcohol intake in the study group

Table 1: Description of sociodemographic details

Sociodemographic parameters	Case (n=30)		Control (n=30)		P-value
	N	%	N	%	
Age					
20–29 years	5	16.7	11	36.7	0.153
30–39 years	10	33.3	10	33.3	
40–50 years	15	50	9	30	
Religion					
Hindu	22	73.3	24	80	0.197
Christian	3	10	5	16.7	
Muslim	5	16.7	1	3.3	
Domicile					
Urban	17	56.7	17	56.7	1.000
Rural	13	43.3	13	43.3	
Marital status					
Married	26	86.7	18	60	0.020
Unmarried	4	13.3	12	40	
Education					
Primary school	7	23.3	7	23.3	0.699
Middle school	18	60	17	56.7	
High school	4	13.3	6	20	
Diploma	1	3.3	0	0	
Occupation					
Unemployed	0	0	1	3.3	0.490
Unskilled	7	23.3	5	16.7	
Semiskilled	11	36.7	7	23.3	
Skilled	9	30	11	36.7	
Clerical	3	10	6	20	
Income					
<2000	0	0	1	3.3	0.231
2000–6000	1	3.3	4	13.3	
6000–10000	13	43.3	7	23.3	
10000–15000	15	50	15	50	
15000–20000	1	3.3	3	10	
Socioeconomic Status					
Lower middle	12	40	17	56.7	0.196
Upper middle	18	60	13	43.3	

Table 2: Comparison of cognitive functions between case and control groups

Parameter	Case (n=30)	Control (n=30)	P-value
Remote memory	7.233±0.935	7.766±0.430	0.006
Recent memory	4.133±0.681	4.400±0.563	0.104
Mental balance	5.200±2.249	6.933±1.284	0.001
Attention and concentration	5.466±2.224	8.933±3.741	<0.0001
Delayed recall	6.633±1.519	7.733±1.460	0.006
Immediate recall	7.400±1.275	8.066±1.257	0.046
Verbal retention for similar pairs	4.166±0.791	4.433±0.568	0.139
Verbal retention for dissimilar pairs	6.200±1.648	7.366±2.092	0.20
Visual retention	6.100±1.936	8.066±2.347	0.001
Recognition	7.533±1.716	8.166±1.116	0.096
Total PGIMS score	60.066±1.936	71.933±2.347	<0.0001

PGIMS: PGI memory scale

(alcoholics). We have reported a significant negative correlation of PGIMS total score with third ventricle width, duration of alcohol consumption, and period of alcohol dependence. In contrast, a significantly positive correlation between PGIMS total score and cerebellar transverse length was observed (Table 4). Likewise, a correlation analysis between parameters of alcohol intake and PGIMS total score indicated a significant negative correlation of PGIMS total score with the quantity of alcohol per day and SADQ score (Table 5).

DISCUSSION

The comparison of individual subtests of the PGI memory scale in our study showed statistical significance in remote memory, mental balance, attention and concentration, delayed recall, immediate recall, and visual retention. A study by Sabhesan et al.,[6] showed similar results that the alcoholics performed poorer than the non-alcoholics. The comparison of individual subtests also showed no statistical significance in recent memory, verbal retention of similar pairs, verbal retention of dissimilar pairs, or visual recognition. The findings were contrary to that observed by Sabhesan et al.,[6] which showed a significant difference in verbal retention of dissimilar pairs between alcoholics and controls.

The total PGI memory score obtained by the case group (6.100) was lower than the control group (8.066). A significant difference between the two groups implies that the alcoholics exhibited cognitive dysfunction more than the controls. The results of Trivedi et al.,[7] supported this finding.

The MRI measurements showed significant differences between cases and controls in measurements of third and fourth ventricle width and interhemispheric fissure width, which implies that ventricular enlargement is more prominent in alcoholics than non-alcoholics. Similar results were noted in the studies of Wilkinson,[8] Lishman[9], and Hayakawa et al.[10] In addition to similar results, the Pfefferbaum et al.,[11] study reported that the dilation was more pronounced in older alcoholics than younger alcoholic men. Rosenbloom et al.,[4] stated that the MRI observations showed a marked loss of brain tissue in alcoholics and added that enlargement of ventricles could be viewed as atrophy of adjacent brain tissues. A study by Ron[12] reported that the size of the ventricular system and interhemispheric fissure width were significantly greater in alcoholics than in non-alcoholics.

The correlation between third ventricle width (a measure of cerebral atrophy) and total PGI memory score showed a significant difference (P=0.001) between cases and controls. The results were coherent with those of Carlen and Wilkinson[13] and Cala and Mastaglia[14] studies. Bergman et al.,[15] and Ron[12] reported that verbal material's immediate and delayed recall appeared more severe in patients with larger ventricles. Significant associations

Table 3: Comparison of MRI measurements between cases and control groups

Parameter	Case (n=30)	Control (n=30)	P-value
Third ventricle width (cm)	0.686±0.685	0.5650±0.56	<0.0001
Fourth ventricle width (cm)	1.669±0.218	1.514±0.152	0.002
Interhemispheric fissure width (cm)	0.409±0.038	0.321±0.042	<0.0001
Cerebellar transverse length (cm)	9.790±0.525	9.794±0.519	0.978
Midbrain diameter (cm)	3.199±0.471	3.106±0.285	0.360
The inner diameter of the skull (cm)	13.007±0.424	12.832±0.463	0.132
Anterior horn distance (cm)	2.914±0.214	2.957±0.261	0.139

Table 4: Correlation between PGIMS total score and MRI measurements in the study group (alcoholics)

Parameter	Pearson correlation coefficient	P-value
Third ventricle width	−0.580	0.001
Fourth ventricle width	0.073	0.701
Interhemispheric width	−0.085	0.655
Cerebellar transverse length	0.422	0.020
Midbrain diameter	−0.100	0.600
The inner diameter of the skull	0.246	0.191
Anterior horn distance	0.210	0.265
Duration of alcohol consumption	−0.644	<0.0001
Period of alcohol dependence	−0.848	<0.0001

Table 5: Correlation between alcohol intake and PGIMS total score

Parameters of alcohol intake	Kendall's correlation	P-value
Frequency of alcohol intake	0.092	0.536
Quantity of alcohol per day	−0.401	0.007
SADQ score	−0.486	0.001

SADQ: Severity of alcohol dependence questionnaire

between intellectual disability and brain atrophy have been found in numerous alcoholic investigations, according to these studies.[16-18] Cognitive impairment may be exacerbated by nutritional shortages and alcohol withdrawal seizures, which are frequently seen in alcohol-dependent individuals.[19]

Lee et al.,[20] failed to elicit any significant correlations between cognitive impairment and neuroimaging findings. Furthermore, Chick et al.,[5] reported minimal evidence of a relationship between cognitive test impairment and measures of atrophy. Our study found no significant correlation between total PGI memory score and parameters such as the inner diameter of the skull, midbrain diameter, anterior horn distance, and fourth ventricle width.

The study has some limitations; the study's small sample size and the female population could not be included due to the scarcity of samples. Furthermore, comorbid personality disorders and the role of benzodiazepines on cognition have not been studied. Thus, its impact on cognitive functions cannot be ruled out.

Limitations of the study

- The study population was derived from tertiary care set up and the number of samples were low. Therefore, generalization of the study results to all clinical settings is not possible.
- The female population could not be included due to the scarcity of the samples.
- Comorbid personality disorders and the role of benzodiazepines on cognition have not been studied, thus its impact on cognitive functions cannot be ruled out.

CONCLUSION

Alcohol-dependent patients performed poorly compared to the controls (non-alcoholics) in all the individual subtests of the PGI memory scale, namely recent memory, remote memory, mental balance, attention and concentration, delayed recall, immediate recall, verbal retention of similar pairs, verbal retention of different pairs, visual retention, and recognition. Alcoholics had significant cerebral and cerebellar atrophy, characterized by dilation of the third and fourth ventricles. Third ventricle dilation decreased their cognitive function in them. The increase in the duration of alcohol consumption, increase in period of alcohol dependence, and increase in severity of alcohol dependence caused cognitive impairment independently.

ACKNOWLEDGMENT

We want to express our sincere gratitude to the patients who took part in this study. Their contribution was invaluable in generating the data and insights presented in this research paper. We also extend our appreciation to the head of the department, as well as the medical staff, for their support and dedication throughout the study. We thank Radiographer Mr.Jeyan for helping us take MRI scan for our patients and calculate the measurements of various parameters analysed in our study.

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Source of Support: Nil, **Conflicts of Interest:** None declared.