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Research Article

Prevalence of Cavum Septum Pellucidum in Alcohol Dependent Patients: A Comparative CT Study

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Abstract

Presence of abnormal cavum septum pellucidum (CSP) in patients of schizophrenia has been reported in many studies. CSP has not been reported in patients of Alcohol dependent syndrome (ADS), though less brain weight and volumespecially of white matter has been found in neuropathological studies. We selected the CT scans,done in the year 2012 and 2013 of male patients of alcohol dependence syndrome and normal controls, who had been referred for CT scanning to the GirindraShekhar Bose Centre for Neuroimaging and Radiological Sciencesof Central Institute of Psychiatry (C.I.P.), Ranchi, for various reasons. We found 54 CT scans of alcohol dependent male patients and 34 CT scans of normal male controls,who satisfiedthe inclusion and exclusion criteria. We defined any CSP greater than or equal to 6mm in length as abnormal. We found significantly increased prevalence of abnormal CSP in alcohol dependent patients (p= 0.007). Similarly, dimension (length and width of cavum and width of septum) of CSP were significantly larger in patient group than controls.

ABBREVIATIONS

CSP: Cavum Septum Pellucidum; CT scan: Computed Tomography Scan; ADS: Alcohol Dependence Syndrome; ICD-10, DCR: International Classification of Diseases-10/Diagnostic Criteria for Research; CIP: Central Institute of Psychiatry

INTRODUCTION

Limbic system along with prefrontal cortex plays an important role in reward-related behaviours of substance dependence [1,2]. Role of reduced volume of amygdala has been noticed in developing alcoholism in high risk individuals [3]. Among different limbic system structures cavum septum pellucidum (CSP) is a marker of limbic system dysgenesis which is due to incomplete fusion of the two leaves of the septum [4].

It is still a debate whether cavumseptiare associated with neuropsychiatric disturbances. A small cavum has been considered as a normal variant (less than 6mm.), but large cavum (=> 6mm)has been found with increased frequency in patients of schizophrenia when compared to normal controls in many studies [5-8].

Though its prevalence in patients of alcohol dependence has not been explored much, only Filipovic *et al.* [9,10] had looked into the differences in morphological features of CSP in autopsied cadavers of patients of alcohol dependence, schizophrenia and traumatized individuals and compared themwith the morphological features of normal cadavers. In alcohol dependent patients, reduced brain weight and atrophy due to reduction in white matter volume, was noticed and it correlated with the amount of alcohol consumed [11]. Changes in myelination and axonal integrity have been stated to be the probable reason for white matter loss [12]. Prefrontal white matter was noted to be the most severely affected region of the brain [13].

In this study we compared the prevalence of normal and abnormal CSP and its dimensions (length of cavity, width of cavity and width of septum) between patients of alcohol dependence and normal subjects using CT scan.

MATERIALS AND METHODS

We selected the CT scans of all patients (aged 18 to 60 years) who had been diagnosed as a case of Alcohol Dependence Syndrome (ADS)in the year 2012 and 2013 as per ICD-10, DCR [14] and who had been admitted in the S.S. Raju Centre for Addiction Psychiatry, C.I.P., Ranchi. Thesepatients had been referred for CT

scanning due to history of complicated withdrawal, history of any type of head injury (significant or insignificant) and for research purpose. We had not selected CT scans of patientsin whom there were any signs of significant head injury, history of neurological illness, systemic illness having potential cognitive consequences, history of any other substance dependence, except nicotine and caffeine and history of any other psychiatric diagnosis.

We excluded all CT scans in which any pathological change was noted. We found 72 CT scans of patients of ADS out of which 7 had history of significant head injury and in 11 CT scans pathological changes were noted. Finally we found 54 subjects who met the study criteria and out of these 54 subjects, 20 had history of delirium and 19 had withdrawal seizures. These patients were all male subjectsbecause we seldom have female dependent inpatient at our centre.

For controls we selected the CT scans of all the male staffof C.I.P. (aged 18 to 60 years) who had undergone CT scanning during the same period and who had no psychiatric diagnosis. These staff members had CT scanning of their brain for minor problems like headache, dizziness and insignificant or minimal head injury.

Any history of neurological illness, significant head injury, and systemic illness with potential cognitive sequele, or current substance abuse or past substance dependence on any other substance except nicotine and caffeine, were excluded from the control group. Finally, we found 64controls including males and females, out of which 34 CT scans of males were included for the study.

We defined significant head injury when there was history of loss of consciousness, amnesia or disorientation and a Glasgow Coma Scale (GCS) score of 13–15 [15,16]. If there was no history of loss of consciousness or amnesia or hospital admission after head injury we defined it as insignificant head injury [17].

For acquiring images Siemens 16 slice CT machine was used. Slices were obtained as per imaging protocol from base of skull through vertex in axial plane. Initially slices were of 4.8 mm in width. Images were further reconstructed at thinner sections, up to 0.75 mm thickness in axial and coronal planes for detailed analysis. The radiologist was blind to the diagnosis. We selected all those scans in which slightest CSP was visible for analysis. Length and width of cavity along with width of septum were measured in the slice with largest dimension of CSP.

For determining and defining prevalence of normal and abnormal CSP we used the criteria that had been used in previous studies [8,18-20]. In these studies any CSP equal to or greater than 6 mm in length had been defined as abnormally large (Picture 1 & 2). CT scans of all patients and controls were reviewed, without knowledge of the diagnostic group by a neuroradiologist and a psychiatrist trained in neuroanatomy. Each rating was assigned on the basis of a consensus between the two examiners.

We also compared the dimensions of CSP in the patients of ADS with and without history of complicated withdrawal.

We used $\chi 2$ (Chi-square) test for categorical variables (presence/absence of CSP and presence/absence of abnormal CSP) and student t- test for continuous variables (dimensions of CSP). Two-tailed $P<0.05$ was considered statistically significant.

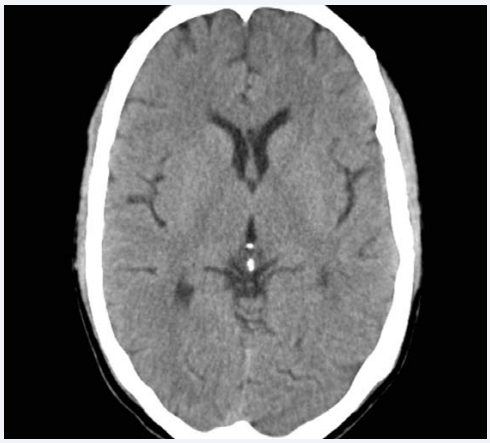

Figure 1 C.T. scan of an alcohol dependent patient showing abnormal CSP (Length 7.0mm, Width 2.8mm, Width of septum 1.6mm)
Abbreviation: CSP: Cavum Septum Pellucidum

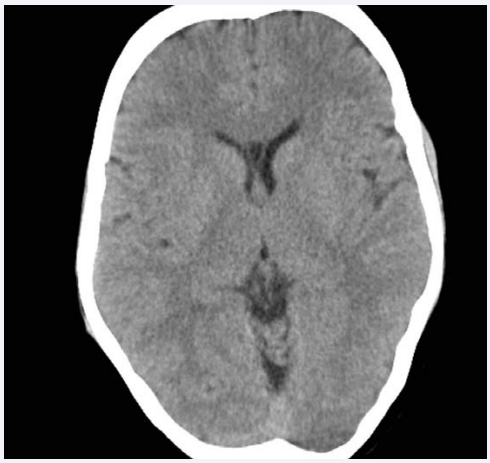

Figure 2 C. T. scan of an alcohol dependent patient showing abnormal CSP (Length 9.6mm, Width 4.7mm, Width of septum 1.2mm)
Abbreviation: CSP: Cavum Septum Pellucidum

RESULTS

From (Table 1), it is evident that mean age and education (no. of years of schooling) of patients and controls were matched. Mean age of patients and controls were 39.15±8.33 years and 39.44±13.38 years respectively, while the years of education were 11.20±3.22 years and 10.68±3.50 years respectively.

The mean age of starting alcohol use in patients was 24.17±7.31 years. When we compared the presence or absence of CSP between patients and controls the difference was significant **(**p= 0.007**)**. Out of a total of 54 patients, 24 patients had CSP (44.4%). In these 24 patients, 10 (18.5%) had CSP less than 6 mm in length, while 14 (25.9%) had CSP equal or greater than 6 mm in length. On the other hand only 4 (11.8%) controls had CSP out of a total of 34, in which 2 (5.9%) controls had CSP less than 6 mm in length and similar number of controls had CSP equal or greater than 6 mm in length (Table 2).

Table 3 shows the comparisons of dimensions (length and

Table 1: Comparison of age & education between patients of ADS and controls.

Variables	Patients (N=54) Mean ± SD	Controls (N=34) Mean ± SD	t value	df	p
Age	39.15±8.33	39.44±13.38	0.127	86	0.899
Education (no. of years of schooling)	11.20±3.22	10.68±3.50	-0.724	86	0.471

*Level of significance accepted at p value of 0.05; **level of significance accepted at p value 0.01; ***level of significance accepted at p value 0.001
Abbreviation: ADS: Alcohol Dependence Syndrome

Table 2: Presence and absence of CSP between patients of ADS and controls.

CSP	Patients N=54 (100%)	Controls N=34 (100%)	χ2 value	df	p
Absent	30 (55.6%)	30 (88.2%)	10.277[f]	2	**0.007****
Present &<6mm	10 (18.5%)	2 (5.9%)			
Present &=>6mm i.e. abnormal CSP	14 (25.9%)	2 (5.9%)			

*Level of significance accepted at p value of 0.05; **level of significance accepted at p value 0.01; ***level of significance accepted at p value 0.001
Abbreviations: CSP: Cavum Septum Pellucidum; ADS: Alcohol Dependence Syndrome

Table 3: Comparison of Dimensions of CSP for patients of ADS and controls.

Dimensions of CSP	Patients (ADS)	Controls	t value	df	p
Length of CSP Mean ± SD (mm)	4.43±8.69	0.61±1.76	-2.519	86	**0.014***
Width of CSP Mean ± SD (mm)	1.26±1.92	0.27±0.76	-2.870	86	**0.005****
Width of septum Mean ± SD (mm)	0.59±0.69	0.16±0.45	-3.268	86	**0.002****

*Level of significance accepted at p value of 0.05; **level of significance accepted at p value 0.01; ***level of significance accepted at p value 0.001
Abbreviations: CSP: Cavum Septum Pellucidum; ADS: Alcohol Dependence Syndrome

Table 4: Prevalence of normal and abnormal CSP in patients of complicated alcohol withdrawal history.

	CSP absent	CSP< 6mm	CSP>6mm	χ2 value	df	p
Delirium						
Absent	18 (60%)	7 (70%)	9 (64.3%)	0.360[f]	2	0.929
Present	12 (40%)	3 (30%)	5 (35.7%)			
Withdrawal seizure						
Absent	22 (73.3%)	7 (70%)	6 (42.9%)	3.860[f]	2	0.149
Present	8 (26.7%)	3 (30%)	8 (57.1%)			

*Level of significance accepted at p value of 0.05; **level of significance accepted at p value 0.01; ***level of significance accepted at p value 0.001
Abbreviation: CSP: Cavum Septum Pellucidum

width of CSP and width of septum) of the two groups. Significant differences were noticed for each of the dimension, with significantly larger dimensions found in patients. The length and width of CSP and width of septum were 4.43±8.69 mm, 1.26±1.92 mm and 0.59±0.69 mm respectively, for patients while that of controls were 0.61±1.76 mm, 0.27±0.76 mm and 0.16±0.45 mm, the p value for each of these dimensions were 0.014, 0.005 and 0.002 respectively.

When we compared the dimensions of CSP in the patients of ADS with and without history of complicated withdrawal no significant difference was found (Table 4).

DISCUSSION

In chronic alcoholism smaller regional brain volumes, functional and metabolic deficits have been observed in different neuroimaging and pathological studies. The commonly involved structures in chronic alcohol dependent patients are frontal and parietal white matter, cortical gray matter, cerebellum, mesial temporal lobe, subcortical structures, corpus callosum, and mammillary bodies [21-24]. Recent neuroimaging studies have indicated loss of brainstem volume particularly in pons [25-28]. No study except for that by Filipovic *et al.* [9,10] had looked for CSP in such patients.

They had found presence of CSP in 58.14% of 25 autopsied alcohol dependent patients, which was more than the prevalence found in our study (44.4%).

The mean dimensions of CSP were significantly larger in patients of alcohol dependence than normal controls. This increased prevalence of CSP in alcohol dependent individuals was not related to presence and absence of history of complicated withdrawal. Prolonged alcohol use seems to be the most probable

reason for increased prevalence of CSP along with significantly abnormal dimensions, since other psychiatric disorders [29,30] which might cause CSP abnormality, were excluded.

Septal area has been recognised for reward behaviours and pleasure for long [31,32]. Some other studies [33] have suggested role of septal nuclei encompassing septum pellucidum and other limbic structures (nucleus accumbens, amygdala, hippocampus and thalamus) in drug sensitization and reinforcement. Hypersensitisation to different substances of this area may lead to addictive behaviours [34]. So it can be said that presence of abnormal CSP may give rise to alcoholism.

Furthermore in the neurodevelopmental model of substance dependence, abnormal development of limbic structures like reduced amygdala volume has been found in later development of alcoholism [3] and abnormal CSP enlargement has been suggested to have a role in early onset of opioid dependence [35].

Chronic alcoholism leads to degeneration of various parts of the brain including demyelination of corpus callosum (Marchiafava-Bignami disease), hemispheric white matterand gray mater [36-39]. Demyelination is due to infiltration of lipid laden macrophages distributed around axons and blood vessels [40]. Due to necrosis, corpus callosumsplits into layers and this could produce cystic lesions with gliotic walls [41].

The increased prevalence of CSP in chronic alcohol dependent patients could be caused by the demyelination and separation of the two laminae of septum pellucidum which might lead to development of cavum [42,43]. This may be another probable explanation which requires further research.

CONCLUSION

Though increased prevalence of abnormal CSP has been noticed in patients of schizophrenia, effect of chronic alcohol use on CSP remains less investigated. This is the first radiological study which looked for the prevalence and change in dimensions of CSP. Our results indicate increased prevalence of CSP along with significantly abnormal dimension (length and width of CSP and width of septum) in patients of alcohol dependence compared to normal controls. The exact reason for this is still to be understood whether presence of abnormal CSPcauses alcoholism as per the neurodevelopmental hypothesis or prolonged use of alcohol gives rise to development of abnormal CSP as per the neurodegenerative model.

The limitations of this study wereselection of only male patients and a retrospective design. CT scans of patients who had been referred for complicated withdrawal and research purposes were studied so generalization of the findings should be made with caution.

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