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THE IMPACT OF LIVER DISEASE ON COGNITIVE FUNCTION

Summery: The current study assessed cognitive function 32 hepatic cirrhosis patients using standardized neuropsychological measures and compared them with types of hepatic cirrhosis by Child Pugh score and the stages of Hepatic Encephalopathy and the same measures of 20 healthy controls. The Study participants underwent a comprehensive neuropsychological battery to assess functioning in the areas of visuospatial, naming, attention, memory, verbal fluency, orientation, abstraction, and also depression, and anxiety questionnaires were completed.

Key words: neuropsychological measures, Hepatic encephalopathy, cognitive deficits

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ВЛИЯНИЕ ЗАБОЛЕВАНИЯ ПЕЧЕНИ НА КОГНИТИВНУЮ ФУНКЦИЮ

Резюме: В текущем исследовании оценивалась когнитивная функция 32 пациентов с циррозом печени с использованием стандартизированных нейропсихологических показателей и сравнивалась их с типами цирроза

печени по шкале Чайлд-Пью и стадиям печеночной энцефалопатии, а также те же показатели у 20 здоровых людей из контрольной группы. Участники исследования прошли комплексную нейропсихологическую батарею для оценки функционирования в областях зрительно-пространственного, именования, внимания, памяти, беглости речи, ориентации, абстракции, а также были заполнены анкеты депрессии и тревоги.

Ключевые слова: нейропсихологические показатели, печеночная энцефалопатия, когнитивные нарушения.

The term “liver disease” (LD) applies to many diseases and disorders that cause the liver to function improperly or stop functioning. Hospital statistics show deaths from LD are increasing. This has serious psychological implications relating to cognitive complaints, reduced quality of life and work-related activities and mental health problems. Hepatic encephalopathy (HE) is understood as a “clinical picture that can present when damage to the brain and nervous system has occurred as a complication of LD”. It is well established that advanced forms of the disease are accompanied by overt and global cognitive deficits (CD). Cognitive impairment (CI) in major depressive disorder have been reported for measures of executive functioning, verbal and nonverbal learning, visuo-motor attention and visuo-spatial process.

Purpose: to study the peculiarity of cognitive function in patients with chronic liver diseases and explore the association between the types and stages of liver diseases and cognitive deficits.

Material and methods: This study was undertaken at the neurological and hepatological departments of ASMI Clinical Hospital. It was based on 32 patients with Hepatic Cirrhosis (HC) (18 men and 14 women) and mean age 54,81 years. The control group (CG) comprised 22 healthy volunteers, mean age 45,59. This group participated in a similar study and served as a CG. Participants were selected after thorough screening of their medical records to exclude any potential risk

factors for CI. We used the following exclusion criteria: illicit drug use or alcohol abuse, current treatment with psychotropic medication, stroke, cancer, cerebrovascular disease, mental retardation, dementia, seizure disorder.

All patients underwent the following:

• Thorough abdominal and Neurological examination.

• Routine investigations as Liver function tests and complete blood picture

• Abdominal ultrasound to determain HC

• Electroencephalography (EEG) was done to all patients .

Patients were subdivided into groups according to the Child Pugh score. Accordingly, 8, 10 and 14 patients were in each of the Class A, B and C respectively. HC was diagnosed by using classical clinical and analytical criteria. For determining the stage of HE was used West-Haven Criteria for HE (latent HE and 1-4 stages). According to it, 5 patients were in latent HE, 8 patients were HE-1, 12 patients were in HE-2 and 7 patient in HE-3. Participants were subsequently, subjected to the Mini-International Neuropsychiatric Interview. The neuropsychological evaluation included:

1. Montreal Cognitive Assessment (MoCA) is cognitive screening tool with proven validity to assist in the detection of CI. The final version of the MoCA used in this study is a 30-point test, including short-term memory recall, executive function tests, sustained attention task, serial subtraction task, digits forward and backward, language tasks, and orientation to time and place.

2. Mini Mental State examination (MMS) is used to assess Orientation to time and place, Instantaneous recall, Short term memory, Serial subtraction or reverse spelling, Constructional capacities (copying a design) and Use of language.

3. Montgomery-Åsberg Depression Rating Scale (MADRS) is designed to measure the degree of severity of depressive symptoms. It is a 10-item checklist. Since there is a comparative lack of emphasis on somatic symptoms, the scale is useful for the assessment of depression in people with physical illness. The following mean scores correlates with global severity measures: very severe, 44; severe, 31; moderate, 25; mild, 15; and recovered, 7.

4. The Hamilton Anxiety Scale (HAS) is a 14-item test measuring the severity of anxiety symptoms. For the 14 items, the values on the scale range from zero to four; according to the severity of anxiety. The total anxiety score ranges from 0 to 56. Persons with generalized anxiety disorder and panic disorder tend to have a total anxiety score of above 20.

Statistical Analysis: The advanced statistical package for social science [SPSS] for MS windows was utilized to furnish the statistical analysis for the study. Simple descriptive statistical tests (Mean and Standard deviation) are used to describe the numerical values of the sample. To test the 2-tailed significance of differences in means, Student t-test for independent samples for 2 groups and one-way analysis of variance (ANOVA) test for comparison between more than 2 groups were used and spearmen correlation test. A probability of (p) $\leq$ 0.05 is accepted as significant.

Results: According to the results of analyses:

	Groups	Measures					
		gener.bil.	direct bil.	indir. bil.	ACT	ALT	PTI
1	Control	12,7±2,7	2,4±0,22	15,2±0,6	0,16±0,02	0,28±0,06	97,8±1,12
2	Latent HE	24,3±1,3	7,5±0,6	16,8±0,8	0,3±0,06	0,7±0,1	44,3±6,9
3	HE1-2	55,1±19,5	21,5±9,6	33,3±10	0,8±0,1	1,4±0,3	56,8±2,07
4	HE 2	49,8±17,9	36,7±10,6	27,5±10,4	0,4±0,05	0,6±0,1	45,3±7,4
5	HE 2-3	26,9±1,1	7,8±0,3	19,1±0,72	0,4±0,04	1,1±0,07	26,9±1,1
6	HE 3	74,5±14,3	28,4±5,1	49,2±7,6	0,7±0,03	1,25±0,08	74,5±14,3

EEG was normal in 18 patients, and showed epileptic form changes in 6 patients; one of them had right focal changes, three showed left focal changes and two with generalized epileptic form changes. None of our patients had triphasic waves. And no significant difference in CF between patients with normal or epileptic form EEG changes.

Regarding neuropsychological tests the patients performed significantly worse than CG in total MoCA score (0.001; 0.005, respectively) indicating mild CI. Naming, memory, attention, Language, fluency, abstraction and orientation were the most affected domains. Visuospatial function and concentration were lower among all patients versus the control but this difference was statistically insignificant. In addition, HC class "C" and HC class "B,A" patients differed significantly in MMS versus the controls (P=0.003; P=0.011, respectively).

The mean score of MADRS and HAS were significantly higher in patient groups than CG (P=0.003; P=0.001 and P= 0.12; P= 0.022, respectively). MADRS scores ranged between zero and 32 (mean=20.42 ±13.62) MADRS was normal in 9 patients, another 8 had recovered depression, 6 mild, 5 moderate and 4 had severe depression, while none of our patients had very severe depression.

With HAS scores there is significant statistical difference between all groups. HAS scores ranged between zero and 29 (mean=11.46±9.11), only 3 patients had scores above 20 which signify anxiety. While 12 were completely normal and the rest of patients had insufficient scores to diagnose anxiety. HC class "C" patients performed poorly all psychometric tests in comparison to other patients but the significant differences recorded in MADRS and HAS scores (P=0.001; P=0.051) but not with MoCA or MMS scores. Also this study reported that there was no correlation between depression, anxiety severity, level of education and neuropsychological test scores in HC class "C" patients.

Discussion: In the present study, a neuropsychological test was administered to patients with LD in order to measure the type and degree of CD. Chronic HC class "C" patients performed significantly worse than healthy CG in all neuropsychometric tests. Also those patients with HC class "A,B" had better performance than those patients with HC class "C" but the difference not statistically significant in MoCA only. There were no differences between these groups when evaluating cognitive domains such affection was higher in dominant hemisphere functions; Visuospatial; attention, naming, memory, Concentration, Language; fluency, abstraction, orientation. The HC class "C" group scored

significantly worse on the power of concentration and on the speed of memory processes than the CG. Depressive and anxiety symptoms have been reported to be common in patients with untreated HC class “C”. The results of this study reveal that all patients had high frequency of some degree of depression and HC class “C” patients had more depressive features than others. These results are in accordance with a previous study that demonstrated HC “C” patients had more depressive features than other groups. Psychological distress and fatigue might also influence cognitive performance, given their high prevalence in people with HC class “C”.

Conclusion: We conclude that chronic HC is accompanied by impairment of cognitive functions. This dysfunction does not appear to be HC class “C” specific, as other patients were found to be similarly impaired. The results from the current study therefore suggest possible deficits in liver also suggest that different patterns of deficits emerge in different severity/stages of LD. The research has therefore provided a basis that can be followed up in future studies in order to understand the patterns and nature of deficits in patients with LD.

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