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Memory Types in Hemodialysis Patients: A Study Based on Hemodialysis Duration, Zahedan, South East of Iran

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***Abstract*—**Neuropsychological problems are more common in hemodialysis (HD) patients than in healthy individuals. The aim of this study was to investigate the effect of long term HD on memory types of HD patients. To assess the different type of memory, we used memory parts of the Persian Papers and Pencil Cognitive assessment package (PCAP) and Addenbrooke's Cognitive Examination (ACE-R). Our study included 80 HD patients of whom 39 had less than six months of HD and 41 patients and another group which had a history of HD more than six months. The population had a mean age of 51.60 years old and 27.5% of them were female. The scores of patients who have been hemodialyzed for a long time (median time of HD was up to 4 years) had lower score in anterograde, explicit, visual, recall and recognition memory (5.44±1.07, 9.49±3.472, 22.805±6.6913, 5.59±10.435, 11.02±3.190 score) than the HD patients who underwent HD for a shorter term, where the median time was 3 to 5 months ($P<0.01$). The regression result shows that, by increasing the HD duration, all memory types are reduced ($R2=0.600$, $P<0.01$). The present study demonstrated that HD patients who were under HD for a long time had significantly lower scores in the different types of memory. However, additional researches are needed in this area.

***Keywords*—**Hemodialysis patients, duration of hemodialysis, memory types, Zahedan.

I. Introduction

HEMODIALYSIS patients are subject to sever hemodynamic changes and large fluid alters during dialysis. This element may increase the risk of acute confusion during dialysis, but the extent to which global cognitive function varies during the dialysis pattern is uncertain. Also, the high problem of cognitive impairment in HD has only recently become recognized [1], [2].

Cognitive function includes: attention, memory, executive function, psychomotor speed, and processing. Memory is one of the important aspects of cognitive functions, which has different types; various aspects of memory have been shown to be impaired: verbal and visual memory [3], [4], working memory [5], recalling new information [6], episodic(explicit) memory [7], recognize [8], immediate memory [9], retrograde memory, and anterograde memory (retrograde and anterograde memory indicate better by anterograde and retrograde amnesia) [10].

Memory is a potential of strength of attention alertness, and concentration together with the duration of these and also fixation takes place in the regular pathways of cortex and subcortical structures of the parietal, occipital, temporal, and frontal lobes [11]. One of the important structures of this pathway is hippocampus and it has been a focal point of memory studies [12].

The verbal memory is one of main cognitive function [13] and verbal memory refers to memory for words, stories, and other verbal things [14]. The moderate correlate of impairments in verbal memory is the degree of hippocampal atrophy on MRI [15]. Also, studies of gray matter density and MRI volumetric have showed the significance of both the perirhinal and entorhinal cortices in aspects of verbal memory [15], [16].

Visual memory refers to the ability to keep and work visual information in mind for a short period of time when it is no longer in view [17]-[19]. Neuroimaging findings have shown that the parietal, frontal cortices, and the early visual cortex can illustrate the specific property information held in visual memory [20]-[22]. Moreover, recent work using an encoding technique represented that in some of the parietal and frontal regions during visual memory maintenance [23].

Working memory relates to a system for short term keeping and manipulation of data, which is essential for difficult cognitive tasks such as reasoning, understanding, and learning [24], [25]. The medial prefrontal cortex plays an important role in the study of emotional and cognitive features of behavior, which is necessary for working memory [26]-[29]. As was said before, hippocampus is the brain structure that is crucial for memory, so inactivation or lesion in this area causes working memory impairment [30]-[33].

Recall is the capacity of remembering the episodic memory based upon a partial or associated sign and it is related to the hippocampus [34], [35]. The recall begins when a sign activates the vestige of an associated memory in hippocampus, and is completed when sensory details of the memory are subsequently restored in neo-cortex [36]. Neo-cortex mechanism is contributing to memory retrieval by indicating the acquaintance of previously faced items or by providing

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sensory details when called upon by hippocampus during recall [37], [38].

Explicit memory is explained as the deliberate recollection of facts or occasions, and needs the integrity of the hippocampus and surrounding cortex of the medial temporal lobe [39]. It is specified by conscious and intentional learning, and needs use of encoded data and recovery tactics which are affected by the individual's general knowledge [40], [41] .

Recognition is the ability to differentiate the incidence of a thing that was previously presented from the one that was not [42]. The neuroanatomical of recognition memory is not unitary process, so in recognition memory process the peri-rhinal cortex, hippocampus, and medial prefrontal cortex involve [43].

The good point of analyzing different types of memory is explained by several theoretical reasons: a) it may allow to understand the final outcome of the different memory types on learning, forgetting, recollection ability, and visual versus verbal memory discrepancies; b) it provides the opportunity to allocate different powers to the severity of different kind of memory performances behind the criteria simply provided by the cut-off; and c) it diminishes the causality error that is obviously more frequent when only general memory is administered [44].

As before said for explaining the anterograde and retrograde memories, it would be better to describe the anterograde and retrograde amnesias. Amnesia refers to a specific, obtained hardly in learning new information and/or getting back information from the past. It is characterized by severe interruption of memory without deficits in intelligence, attention, perception, or judgments [45].

There are two main classes of amnesia; anterograde, and retrograde. Anterograde amnesia is such memory impairment and it is the loss of the ability to create new memories after the accident, in another word, inability to recall the recent past, while long-term memories from before the event remain intact. On the other hand, retrograde amnesia is the impairment of memory new memories can be formed, but old memories are lost. It means the loss of memory-access to events that occurred or information that was learned, before an injury or the onset of a disease. By this explanation, one can say that the retrograde memory is the ability of remembering the old things that happened before [45].

That bilateral lesion in the hippocampus and related medial temporal lobe (MTL) structures, the perirhinal, entorhinal and parahippocampal cortices, lead to serious anterograde amnesia [46]. However, there is considerable argue concerning the effects of damage to this region like: the damage must extend to extra-MTL structures to make a temporally extensive retrograde amnesia [47], [48]. Though, Poreh et al. (2006) showed that bilateral lesions in the fornix lead to anterograde and retrograde amnesia without significantly affecting other cognitive functions [46].

The study of different functions of memory is important because decreased memory domains may compromise an individual's quality of life, rise resource usage and outcome in suboptimal medical attention. Also, few studies have focused on memory types in renal patients; most of them suggested a high prevalence of cognitive impairment compared with the general population in general [49]-[51].

II. Subjects

We had about 98 HD patients aged 40 to 70, but only 80 people responded and entered the research. It should be noted that patients with myocardial infarction, stroke, cerebral surgery, epilepsy and depression were excluded from the study. Data were collected from Alie-Ebne- Abitaleb and Khatamol-Anbia hospitals, in Zahedan, South-East of Iran.

III. Methods

The data were analyzed by SPSS version 20 (SPSS Inc., Chicago IL, USA). Standard descriptive statistics were applied to examine baseline demographic characteristics and cognitive values. Descriptive statistics were reported as mean ± standard deviation (SD) for continuous variables and as frequencies and proportions for categorical variables. Independent sample T-test was used to compare the groups and to show relation regression which had been used.

IV. Study Protocol

At first, two groups of HD patients from Alie-Ebne-Abitaleb and Khatamol-Anbia hospital were selected. Patients were divided into two groups; (1) patients who were under HD less than six months and (2) patients who were under HD over six months.

The Beck depression test was conducted to determine whether patients had depression, to ensure that different memory functions are not the result of symptoms of depression in patients. Before the Neuropsychology tests, blood samples were taken to ensure that the patients are in the same situation. Blood samples were collected before evaluating memory in HD patients; the following factors were measured: white blood cell, red blood cells, hemoglobin, hematocrit, mean corpuscular volume, mean corpuscular hemoglobin, mean corpuscular hemoglobin concentration, platelets, red blood cell distribution width, mean plackets volume, platelets larger cell ratio, blood sugar, blood urea nitrogen, serum creatinine, sodium, potassium, calcium, alkaline phosphatase and phosphorus.

Memory types were tested 24 hours after the last HD using The PCAP and the ACE-R.

From the PCAP, visual memory and verbal memory tasks and from ACE-R, recall, immediate memory, delayed memory, recognize, retrograde memory and anterograde memory tasks were used to gather information on socio-demographic data and memory information. The instrument was administered by trained health in the language (Dr. Hamed Ekhtiari and Dr. Hamidreza Pouretemadi) best understood by participants. The study was conducted over a 12- month period (March 2016 and April 2017). In addition, each participant signed consent form before they were admitted into the study. Ethics approval was also received from Zahedan University of Medical Sciences and ethics

committee. Also, during the study, patients would be excluded from research if they did not consent to continue their research (proposal cod: 7760). The results of this study were presented to the patients.

V. Results

The data were available for 80 individuals. Table I shows demographic and clinical characteristics of study participants. The 63.8% of patients were ≥55 years of age. The 72.5% of patients were male. Most of patients had under middle school degree 36 (45%), 20 (25%) patients had academic degree (associate, bachelor, master and PHD degree). The HD duration in 39 (48.7%) patients was under 6 months and 41 (51.3%) in patients over 6 months.

TABLE I
Demographic and Clinical Characteristic among Studied Population

	Variables	Frequency	Percentage	Mean± SD
Age	>6 Month	39	48.8%	49.77±9.15
	<6 Month	41	51.3%	53.34±8.08
	Total	80	100%	
Sex	Male	58	72.5%	
	Female	22	27.5%	
	Total	80	100%	
EDU	Under Middle School	36	45%	
	High School Diploma	24	30%	
	Associate's Degree	2	2.5%	
	Bachelor's Degree	16	20%	
	Masters or PHD	2	2.5%	
	Total	80	100%	
HD	>6 Month	39	48.8%	
	<6 Month	40	51.3%	1.51± 0.503
	Total	80	100%	

Abbreviations: HD, hemodialysis duration; EDU, education

The variables (visual memory, verbal memory, recall, immediate, delayed, recognize, retrograde ad anterograde memory) used to evaluate memory in HD patients are demonstrated in Table II.

TABLE II
Variables Which Evaluated Memory in HD Patients

	HD Duration		
Variable	<6 Months	>6 Months	P value
	Mean ± SD	Mean± SD	
RM	6.33±.772	5.44±1.07	.031
AM	3.13±.695	2.78±.652	.969
VEM	11.90±2.469	9.49±3.472	.001
VIM	33.179±3.7196	22.805±6.6913	.001
IM	21.974±6.8171	13.073±5.8562	.218
DM	21.29±5.989	13.02±5.409	.354
Recall	15.97±5.338	5.59±10.435	.010
Recognize	13.08±2.145	11.02±3.190	.001

Abbreviations: RM, retrograde memory; AM, anterograde memory; VEM, verbal memory; VIM, visual memory; IM, immediate memory; DM, delayed memory.

The results showed that retrograde memory in patients who were under HD for less than six months was higher (6.33±.772) compared to patients who were under HD for more than six months (5.44±1.07) (P=0.031). Additionally, verbal memory mean score in less than six months patients was higher (11.90±2.469) than patients who had been under longer term HD (9.49±3.472) (P=0.001). Moreover, visual memory mean score in patients who had shorter duration of HD was significantly more than longer term ones (33.179±3.7196 versus 22.805±6.6913). Recognized score in patients under HD of less than six months was higher (13.08±2.145) than patients that under HD of more than six months. Similarly, in anterograde memory, immediate memory, delayed memory and recall task less than six months patients scores were higher (33.179±3.7196 ،21.974±6.8171 ، 21.29±5.989 ،15.97±5.338 ،13.08±2.145) compared to the one up to six months.

TABLE III
Regression Analysis of HD Duration with Attention and Memory in HD Patients

Model1(HD Time)			
dependent variable	F	Beta	P
RM	5.327	-.253	.001
AM	18.133	-.434	.001
VEM	12.681	-.374	.001
VIM	72.432	-.694	.001
IM	39.367	-.579	.001
DM	42.094	-.592	.001
Recall	30.938	-.533	.001
Recognize	11.290	-.356	.001
R2		.600	
Adjusted R2		.561	

The result of regression test presented in Table III shows that the relationship between the duration of HD as independent variable with all variables significantly inverse. As the HD time increases, retrograde memory, anterograde memory, verbal memory, visual memory, immediate memory, delayed memory, recall and recognize decrease.

VI. Conclusion

In summary, our findings suggest that HD adult patients have high rates of memory impairments. Furthermore, these impairments are most pronounced in persons aged 61 and older and are not associated with other pervious illnesses such as: cardiovascular disease, neurological diseases, brain surgery and depression. The present study confirms the literature, which notes that subjective memory concerns are related to cognitive impairment, and they did not have association with depression.

Approximately 2 fourth of these participants had completed elementary school, 1 fourth had completed high school, and 1 fourth had completed college and the men were about twice than women. These findings are significant because some researches indicated that people with low education vulnerable to Alzheimer's disease related pathology and perform worse on cognitive assessments [52], [53], also according to some studies females surpass in verbal tasks, perceptual speed and in memory and verbal learning tasks [54], [55], which

corresponds to our findings; however, the gender ratio was not equal in the present study.

We showed that long-term HD in all types of memory (retrograde, anterograde, verbal, visual, immediate, delayed memory, recall and recognize) had lower scores than patients who recently started HD. Also, there were negative relationships between the duration of HD and memory varieties. Hence, this issue is worth mentioning, it could be an increase rate of dementia, specially Alzheimer disease in this group of people as Abdelrahman et al. (2014) suggested that 23% of HD had mild dementia, 8.5% of patients had moderate dementia, and 7.4% of them had severe dementia [56].

The remediation efforts for improving memory impairment in HD patients is vital; however, it is uncertain whether cognitive rehabilitation can refine different type of memory impairments in HD patients, but neuropsychological rehabilitation in these patients particular, may play a role in improving the memory functions or in the individual's potential to adapt to the problem. Remediation efforts have often included (1) cognitive remediation, that controls drill-and-practice exercises using repeatable batteries of neuropsychological tests to improve cognition [57], and (2) functional remediation, which manages neuropsychological education about how to adapt around cognitive deficits beside exercises using these strategies in their life [58].

Also, these results suggest that HD patients might be progressively compromised in the memory varieties during HD period. The findings have important implications for medical management of HD patients, and highlight the need for further investigation about different memory types in this group of patients. Developing a better understanding of the factors underlying neuropsychological performance in HD patients is crucial to detect persons who may be at risk of Alzheimer disease years before the initiation of dialysis to identify and treat potentially reversible causes of memory dysfunctions, and to provide essential support to manage complicated medication and dietary regimens.

This study was cross sectional and one of the limitations was unsuited for determining causality of decreasing memory types in HD patients and cohort survey does not have this defect. Another important limitation was the lack of a gold standard to identifying when the memory reduction intensifies.

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