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Progression of cognitive impairment in hemodialysis patients

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Abstract

Objective: Cognitive impairment increases the risk of mortality in patients with chronic kidney disease. Progressive cognitive decline can be a serious issue for hemodialysis patients even if they are young with few comorbid conditions. This prospective study aims to evaluate hemodialysis patients using the Montreal Cognitive Assessment (MoCA) and search for the signs of cognitive decline using cognitive domain scores.

Method: Twenty-nine chronic hemodialysis patients were selected. All patients were tested with MoCA at baseline and after the two-year follow-up. Patients with heart failure, dementia, depression, visual disturbance, malignancy, active infections, and those with single-pool Kt/V<1.4 at baseline or during follow-up were excluded. Patients with MoCA global score <24/30 are considered to be cognitively impaired. MoCA and MoCA subscale scores were compared for differences in time.

Results: The number of patients with cognitive impairment at baseline increased from 18 (62%) to 22 (75.8%) after 2 years follow-up period. The mean total MoCA score after follow-up was significantly lower than that of the baseline (20.57±4.64<22.17±3.87; p=0.001). Analysis for MoCA subscale scores revealed that the mean scores for the attention and language cognitive domains were significantly lower in the follow-up measures compared to the baseline measures in hemodialysis patients (p=0.013 & p<0.001).

Conclusion: This study demonstrated that global cognitive scores in hemodialysis patients decrease over time. This cognitive decline was predominantly related to the differences in attention and language scores. Routine comprehensive evaluation of hemodialysis patients with cognitive batteries may be helpful in detecting the progression of cognitive function.

Keywords: Cognitive impairment, end stage renal disease, hemodialysis, attention, language

INTRODUCTION

Cognitive impairment (CI) describes the decline in cognitive abilities classified as executive function, language, attention, memory, and orientation. Major neurocognitive disorder (NCD) is described as a gradual decline in all cognitive domains that results in a decreased ability to function independently. Mild NCD is an early stage of cognitive deterioration beyond the expected decline of normal aging (1). Since NCD is an umbrella term, it is important to define the underlying neurological, neuropsychiatric, and/or medical disorders (2).

Chronic kidney disease (CKD) is one of the most common medical disorders that can lead to cognitive impairment which may result in major NCD. The incidence of cognitive impairment in CKD is nearly four times the general population (3). Pathophysiology of CKD-related cognitive impairment is mainly associated with atherosclerosis and small vessel cardiovascular disease (CVD). In patients with CKD, vascular aging, metabolic abnormalities, chronic inflammation, and comorbid conditions like diabetes mellitus (DM), and hypertension lead to occult cerebrovascular disease (4). The presence of low estimated Glomerular Filtration Rate (eGFR) and high albuminuria were shown to be independent risk factors for developing cognitive impairment in patients with CKD (5,6). In patients with advanced CKD increased uremic metabolites, vascular calcification, anemia, polypharmacy, intradialytic hypotension, and anticoagulant-associated cerebral microbleeds may contribute to cognitive impairment

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Progressive cognitive impairment would cause hemodialysis patients to be reckless and unaware of the risks of their medical condition. Even though it is known to be progressive and associated with increased mortality, cognitive impairment is usually overlooked, especially in chronic hemodialysis patients. The literature data about hemodialysis patients with CI indicates that vascular burden and intradialytic factors may affect the frontal brain (10). This kind of CI usually leads to a decline in the executive functions of the brain, without affecting praxis or memory. There are several types of cognitive tests used to assess NCD. Among them, the Montreal Cognitive Assessment (MoCA), is widely used in clinical practice and it is validated in patients with CKD (11,12). This prospective study aims to evaluate hemodialysis patients using MoCA and search for the signs of progressive cognitive decline using cognitive domain scores.

METHOD

Patient selection

This prospective time trend study was conducted in the hemodialysis unit of the Nephrology Department at Kahramanmaras Sutcu Imam University between April 2018 - May 2020. The study was approved by the Local Institutional Ethics Committee of the Faculty of Medicine at Kahramanmaras Sutcu Imam University (ethical approval ID: 2018/05 - 16). Participants were given information about the study and agreed by signing a consent form. The study followed the ethical standards of the Declaration of Helsinki.

Patients were selected according to the following criteria, inclusion; chronic hemodialysis patients between 18 and 65 years of age, exclusion; active infection, visual disturbance, thyroid dysfunction, severe anemia (hemoglobin < 9 g/dL), dialysis inadequacy (single-pool Kt/V value of the Daugirdas formula <1.4), diagnosis of heart failure, dementia, psychosis or cerebrovascular disease (13). The baseline study started with 34 adult patients who were on maintenance hemodialysis, three-times per week. During the two-year follow-up period, one patient passed away, one patient was diagnosed with cerebrovascular disease, and three patients moved to other cities. Therefore, we ended up with 29 participants who met the inclusion and exclusion criteria at baseline and after two years. These patients resided in the same region and continued their routine hemodialysis treatment within the same facility. Patients received hemodialysis treatment via their arteriovenous fistulas or tunneled/cuffed catheters. The duration of dialysis was 4 hours for each session with conventional heparinization and a blood flow rate of 250-400 mL/min. The known etiologies for CKD among the study subjects were; hypertension (37.9), DM (20.6%), glomerulonephritis (13.7%), polycystic kidney disease (10.3%), and amyloidosis (6.8). All patients were seen in the dialysis unit three times a week and any complaints that could affect their cognition were noted.

Cognitive assessment and data collection

All subjects were evaluated with the MoCA test (original version 7.1) at baseline and after a two-year follow-up period. Cognitive tests were performed in a separate room, just before a midweek hemodialysis treatment session (14,15). The total MoCA test score is calculated as 30 points. It includes variable cognitive domains, 5 points of visuospatial/executive, 3 points of naming, 6 points of attention, 3 points of language, 2 points of abstraction, 5 points of memory, and 6 points of orientation. Hemodialysis patients with MoCA global score <24/30 were considered cognitively impaired (15,16). The change in MoCA global and MoCA subgroup results before and after two years were analyzed comparatively. Comorbidities (DM, hypertension, & CVD), educational status (number of years), and body mass index (BMI-kg/m2) of all patients were recorded. Relatives and/or caregivers of the patients who scored below 24/30 were informed about the situation and adherence to their medical treatment was improved with the help of a dietitian and a social services specialist.

Statistical Analysis

IBM SPSS software, version 19.0 (IBM Corp., Armonk, NY) was used for the analysis of the data. Values were recorded as mean±SD or %. Chi-square and Fischer's exact tests were utilized for the analysis of categorical variables. The normality of distribution in continuous variables was evaluated with the Shapiro-Wilk test. Student's t-test and Mann-Whitney-U test for the comparison of continuous data.

RESULTS

Clinical data details

The study included 29 hemodialysis patients. The mean age at baseline was 43.79±11.6 years. The Mean education period was 8.72±3.83 years, and the mean MoCA global cognitive score at baseline was 22.17±4.00. In this initial cognitive evaluation, 18 patients (62.0%) had CI (MoCA score <24/30). The mean follow-up period of the patients was 25.17±1.28 months. Almost half of the patients had hypertension. The baseline demographics of the study population are shown (Table 1).

Comparative analysis of follow-up cognitive test scores

After the two-year follow-up, the number of patients with CI increased from 18 to 22 (75.8%). This increase in the

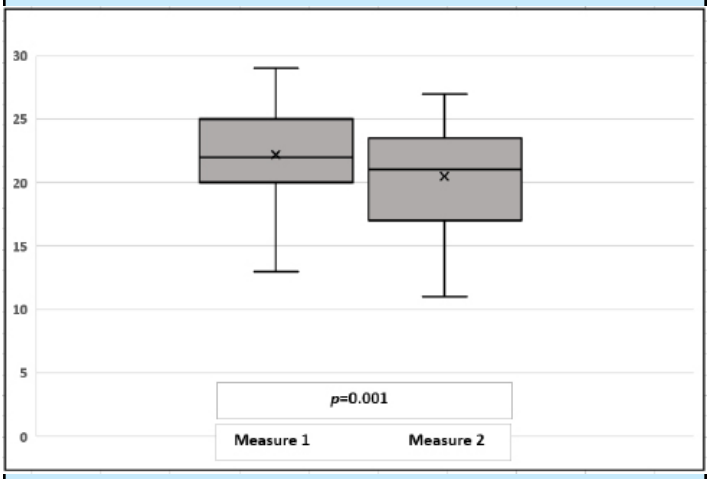

Figure 1. Comparison between baseline and two-year follow-up Montreal Cognitive Assessment global scores

Table 1. Baseline demographics of the study population

Variable	Hemodialysis patients (n = 29)
Age; years ±SD	43.79±11.06
Gender; male/female (%)	19 (65.5) / 10 (34.5)
BMI; kg/m² ±SD	23.10±3.21
Education; years ±SD	8.72±3.83
MoCA global score ±SD*	22.17±4.00
DM; n (%)	6 (20.7)
Hypertension; n (%)	14 (48.3)
CVD; n (%)	6 (20.7)
Hemodialysis vintage; months ±SD	55.34±47.20
Follow-up period; months ±SD	25.17±1.28

Abbreviations: BMI, Body mass index; MoCA, Montreal cognitive assessment; DM, Diabetes mellitus; CVD, Cardiovascular disease. *Baseline mean cognitive test score of the participants.

Table 2. Mean cognitive domain scores at baseline and after two-year follow-up (n=29)

Cognition (Max. score)	Measure 1	Measure 2	p value
MoCA global score (30)	22.17±4.00	20.57±4.03	0.001
Visuospatial / executive (5)	3.10±1.39	3.37±1.26	0.124
Naming (3)	2.76±0.43	2.62±0.56	0.157
Attention (6)	5.17±1.00	4.55±1.24	0.013
Language (3)	2.03±1.11	0.96±0.86	< 0.001
Abstraction (2)	1.34±0.76	1.00±0.80	0.072
Memory (5)	2.07±1.43	2.20±1.61	0.641
Orientation (6)	5.79±0.41	5.79±0.49	1.000

Abbreviation: MoCA, Montreal cognitive assessment

number of CI patients did not constitute a statistically significant impact (p=0.125). However, a statistically significant decline in the MoCA global score from 22.17±4.00 to 20.57±4.03 was observed after the follow-up period (p=0.001) (Figure 1).

After evaluating the MoCA global scores, the MoCA subscale domain scores of the hemodialysis patients were compared. This analysis revealed that the decline in MoCA global score over time was mostly associated with the declining scores for attention and language domains (p=0.013, p<0.001, respectively). The comparative scores of all MoCA domains at baseline and after follow-up in hemodialysis patients are shown in (Table 2).

DISCUSSION

Cognitive impairment is associated with all-cause mortality in patients with advanced CKD (17). Cognitive decline in hemodialysis patients is generally progressive. Early detection of cognitive decline may provide the time to prevent this progression to major NCD. In this study, it was shown that global cognitive scores decrease significantly over time in hemodialysis patients. More than that, the findings of this study indicated that language and attention domains of cognition may be impacted in young hemodialysis patients without evident cerebrovascular disease.

Evaluation of cognitive impairment is delving into the limitation of mental functions and abilities. We evaluated hemodialysis patients at baseline and after two years with MoCA, which is a sensitive testing tool (12,14,16). The percentage of patients with cognitive impairment increased after the follow-up period even if the difference was not significant. If the study sample size was larger, it would have been possible to demonstrate an increased number of patients with a MoCA cut-off value of < 24/30. We selected the 24-cut-off value instead of the standard 26, to prevent the overestimation of cognitive impairment in the hemodialysis population. This lower cut-off was validated in CKD patients for the evaluation of frontal and temporal lobe functions (15).

The important aspect of this study is that we recorded cognitive domain scores at baseline and after two years which was a suitable follow-up period considering the annual mortality rates in the hemodialysis population. Previous studies showed that executive, attention, language, and orientation domains of cognition may be adversely

affected in patients with advanced CKD (16-18). The results of this study revealed that attention and language subscale scores decreased significantly after follow-up, indicating a progressive cognitive decline. As we expected memory domain scores were similar to the baseline values. In previous studies, the memory function had the slowest rate of decline in CKD patients compared to other cognitive domains (17). Contrary to our expectations, executive cognitive scores did not decrease over time. This may be due to the low number of diabetic patients in our study sample.

Cognitive impairment increases with aging. Besides aging, prolonged hemodialysis vintage may be a contributor to CI in the hemodialysis population. The prevalence of CI in hemodialysis patients has been reported to range from 60% to 80% (18,19). We studied with young adults and the prevalence of CI observed in this study is consistent with the aforementioned findings. Although cognitive impairment is so common in the hemodialysis population, it is rarely diagnosed in young dialysis patients. Young patients and patients with high educational status tend to mask their cognitive deficits. Therefore, cognitive test tools are useful for uncovering occult cognitive dysfunction.

It should be noted that the CI associated with CKD differs from that associated with dementia and senility (2,20,21). The precise underlying mechanisms remain unclear but occult cerebrovascular disease is the main explanation. Other than vascular disease, a variety of risk factors have been identified that may contribute to the development of cognitive dysfunction in hemodialysis patients. Accumulation of uremic solutes, hypertension, intradialytic hypotension, fatigue, and anemia, may impair cognitive functions in hemodialysis patients (20,22,23). To avoid false measurements and confounding results, we designed the exclusion criteria to be comprehensive. For that, cognitive tests were implemented before a midweek hemodialysis session, and patients with heart failure, anemia, and dialysis inadequacy were not included. Our analysis did not reveal a significant correlation between the decrease in MoCA scores and the presence of comorbidity. Given our limited sample size, the likelihood of establishing such a connection was reduced. The strengths of this study are the implementation of detailed exclusion criteria, the inclusion of younger patients, and the comparison of follow-up data.

Limitations of the study

The main limitations of this study are that it is a single-center study and the sample size is rather small.

CONCLUSION

Hemodialysis patients are at risk for progressive cognitive impairment even at young ages. In this follow-up study, we evaluated young adult hemodialysis patients for cognitive performance. This study demonstrated that cognitive decline may affect attention and language domains generally preserving memory function. Routine evaluation for cognition may reveal occult cognitive impairments in hemodialysis patients. A multidisciplinary approach is necessary for the treatment of progressive cognitive decline.

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Peer-Review

Both externally and internally peer reviewed.

Conflict of Interest

The authors declare that they have no conflict of interests regarding content of this article.

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Ethical Declaration

Ethical permission was obtained from the Kahramanmaras Sutcu Imam University, Medical Faculty Clinical Ethics Committee for this study with year 2018 and number 05/16, and Helsinki Declaration rules were followed to conduct this study.

Authorship Contributions

Concept: EE, Design: EE, IO, Supervising: EE, NE, Financing and equipment: GA, NE, Data collection and entry: GA, NE, IO, Analysis and interpretation: EE, OA, Literature search: EE, GA, NE, IO, Writing: EE, NE, IO Critical review: EE, NE, OA.

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