ORIGINAL ARTICLE

Title

Effect of a Single Dialysis Session on Cognitive Function in Chronic Kidney Disease Stage 5 Hemodialysis Patients

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*Received 7 April 2019, revised 1 July 2019, accepted 17 July 2019, published 1 August 2019***Abstract**

Background: The incidence of cognitive impairment (CI) has been widely reported in various studies among chronic kidney disease (CKD) patients. Many factors influence cognitive function including the hemodialysis (HD) process itself. There is much evidence that a single HD session brings about changes in the cognitive status of patients, but just a few studies assessing whether cognitive performance varies with dialysis.

Aim: To know the effect of single dialysis session on cognitive function in HD patients.

Method: Sixty medically stable CKD stage 5 patients on HD maintenance for at least three months were enrolled. Cognitive testing performed thrice, 1-2 hour prior to dialysis (T1), 3-4 hour into the session (T2) and 24 hour after the session (T3) using a well-validated neuropsychological test battery, Montreal Cognitive Assessment (MoCA) Indonesian version which assess the domain of cognitive function including visuospatial, executive function, naming, memory, attention, language, abstraction, recall, and orientation.

Result: Subjects' mean age was $45,45 \pm 11,28$ years, dialysis vintage $10,12 \pm 11,88$ months, 44 patients (73,3%) had CI at baseline. Cognitive function decline during dialysis (T2) (MoCA INA score 21,65 to 19,67, $p < 0.001$) and visuospatial, executive function, attention, language and recall was impaired during dialy-

sis. Cognitive function reached its best 24 hour after dialysis (MoCA INA score 23,65, $p < 0.001$) and all the domain of cognitive function was improved except naming that didn't change over the dialysis session.

Conclusion: There is an effect of single HD session on global cognitive function where executive function, attention, language, and recall deteriorated during HD while abstraction and orientation didn't change. All cognitive domains were recovered 24 hours after HD except naming that didn't change from baseline throughout the whole process.

Keywords: cognitive function, chronic kidney disease, hemodialysis

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Introduction

Chronic kidney disease (CKD) is a major public health problem varying in severity from asymptomatic to end stage renal disease (ESRD) requiring hemodialysis (HD).¹ Patients with CKD are frequently associated with neurological complication. Common neurological

Participants and Setting

The design of this study was cross-sectional. Patients were selected among those attending the HD unit of Dr. Wahidin Sudirohusodo General Hospital, Makassar from June – October 2018. Inclusion criteria were patients over the age of 18 years old, medically stable, and willing to participate in the research, being on HD maintenance for at least 3 months, twice to thrice a week. Exclusion criteria were patients over the age of 60 years old because dementia is reported common over this age, unconscious, vision and hearing impairment, unable to read and to write, severe mental disorder, and consuming narcotics, psychotropic, and addictive drugs.

Neuropsychological Assessment and Clinical Variables

Cognition was assessed in a quiet and spacious room with adequate lighting and using a screen to isolate patients for privacy. Cognitive test was done using a well validated neuropsychological test, the MoCA INA tool.^{18,19} It assess 8 cognitive domains, generating a score of between 0 to 30 – Visuospatial/executive function (5), naming (3), memory (0), attention (6), language (3), abstraction (2), delayed recall (5) and orientation (6). Cognitive impairment was defined as MoCA INA score < 26.

Cognitive test was done thrice, T1 was done 1-2 hour before the start of HD, T2 was done 3-4 hour into the session in the same day of T1, and T3 was done 24 hours after the HD session. For each assessment, the patients were allowed up to 30 minutes. All patients were dialyzed in the morning and afternoon, no medications were administered during dialysis except paracetamol, erythropoietin, and blood transfusion if required.

Patients who were the subject of the study underwent an examination starting with anamnesis to get the socio-demographic details (age, sex, and years of education), medical history, current medication, and comorbidities. Clinical data also included dialysis vintage, duration of each dialysis session, blood flow rate (QB), ultrafiltration volume (UF). We also did physical examinations including pre- and post-dialysis body weight, pre- and intra-dialysis blood pressure (BP). We also obtained some laboratory testing including hemoglobin (Hb), plasma glucose, albumin, urea and creatinine, and electrolyte (all taken pre dialysis except for urea that was taken also at the end of the dialysis session to calculate

complications in CKD include stroke, cognitive impairment (CI), encephalopathy and peripheral neuropathy.^{2,3} Cognitive impairment in patients with CKD are frequent and show increasing prevalence rates. Several risk factors such as uremia, anemia, fluid and electrolyte disorder, related comorbidities include hypertension (HT), diabetes mellitus (DM) and cerebrovascular diseases have been linked to cognitive decline.⁴⁻⁸

HD process itself has also been suggested as the potential cause of CI. Potential HD-specific mechanisms include acute fluid shift, dialysis disequilibrium syndrome and brain micro-bleeding due to anticoagulant during dialysis. However, there are also biochemical change induced by HD that potentially lead to cognitive improvement including uremic toxin elimination, correction of fluid and electrolyte disorder and partial correction of anemia. This mechanism possibly cause a fluctuation of cognitive function over a single HD session.⁹⁻¹¹

Cognitive function is needed to access health services, process, understand, and recall written and spoken information and assimilate and express decisions about health care.¹² Impaired cognition has been linked to reduced health literacy, decreased medication adherence, impaired physical and mental health, and greater risk for death.¹²⁻¹⁴ Therefore, even when cognitive improvement is temporary, such as after dialysis or between dialysis, it is important to sustain a good quality of life.¹¹

There have been few studies examining cognitive function following a single dialysis session. The majority of studies had established that cognitive performance of HD patients was best approximately 24 hours after the last HD session compared to shortly before the session.^{15,16} To our knowledge, there was just one study with a small sample size that conducted cognitive tests during dialysis and at other times to measure acute variations in cognitive function during the dialysis cycle.¹⁷ In addition, there was no study assessing the cognitive function of HD patients in Indonesia in recent years.

Hence the aim of this study was to assess the effect of a single HD session on cognitive function using the Indonesian version of well-validated neuropsychological test battery, Montreal Cognitive Assessment (MoCA INA).

Materials and Methods

urea reduction rate [URR] and Kt/V). The protocol of the study was informed to all subjects regarding the risks and benefits of the study. Informed consent was acquired from all subjects.

Result

Subject characteristic

Sixty CKD stage 5 patients on maintenance HD completing all three cognitive testing were recruited. The mean age was $45,45 \pm 11,28$ years, 31 patients (51,7%) were male, 41 patients (68,3%) with education level ≤ 12 years, dialysis vintage $10,12 \pm 11,88$ months, 50 patients (83,3%) with non adequate HD. Socio-demographic and medical characteristics of the study participants are shown in table 1 and 2.

In this study, mean change of systolic BP $-1,33 \pm 12,55$ mmHg, mean change of diastolic BP $-3,67 \pm 10,8$ mmHg, 10 patients (16,7%) had hypotension (systolic BP drop ≥ 20 mmHg or MAP drop > 10 mmHg) during dialysis. Mean change in bodyweight over dialysis $-1,55 \pm 0,70$ kg. Blood flow rate during dialysis 120-300 ml/min (mean $177,17 \pm 26,69$ ml/min), ultrafiltration volume 500-3.500 ml (mean $1.798 \pm 708,18$ ml), range of Kt/V 0,24-2,06 (mean $0,94 \pm 0,41$) while URR range from 15,46-97,17 (mean $52,67 \pm 17,24\%$).

Table 1. Subject Characteristic (n=60)-Part 1

Variable		n	%
Sex	Men	31	51,7
	Women	29	48,3
Age (years)	18-40	17	28,3
	41-60	43	71,7
Education (years)	≤ 12	41	68,3
	> 12	19	31,7
Dialysis Vintage (months)	< 6	33	55,0
	6-12	27	45,0
HD Frequency (time/week)	3	45	75,0
	2	15	25,0
Duration in HD (hours)	4	56	93,3
	5	4	6,7

Table 2. Subject Characteristics-Part 2

Variable	Min	Max	Mean	SD
Age (years)	18	60	45,45	11,28
Dialysis Vintage (months)	3	60	10,12	11,88
Pre HD Weight (kg)	35	85	54,62	9,96
Post HD Weight (kg)	34	83	53,07	9,86
Change in Weight (kg)	-3	0	1,55	0,70
Pre HD Blood Pressure (mmHg)			150,83/83,67	18,80/13,65
Intra HD Blood Pressure (mmHg)			149,5/80	21,10/14,61
Change in Systolic BP (mmHg)	-30	30	-1,33	12,5
Change in Diastolic BP (mmHg)	-40	20	-3,67	10,89
Blood Flow Rate (QB) (ml/min)	120	300	177,17	26,69
Ultrafiltration Volume (ml)	500	3500	1798,33	708,18
Kt/V	0,24	2,06	0,94	0,41
URR (%)	15,46	97,17	52,67	17,24
Hb (gr/dl)	5,1	11,0	8,04	1,30
Albumin (gr/dl)	2,0	4,3	3,18	0,54
Plasma Glucose (mg/dl)	65	288	121,45	45,59
Sodium (mmol/l)	126	146	138,23	4,43
Potassium (mmol/l)	3,3	6,7	4,56	0,75

Cognitive test

Forty four patients (73,3%) had CI before the start of HD session (T1) (MoCA INA score < 26) while during HD (T2) the participant who had CI increased to 55 patients (91,7%) and 24 hr after HD (T3) the participant who had CI decreased to 37 patients (61,7%) (Table 3).

The total MoCA INA score T2 was significantly lower than T1 (19.67 to 21.65 ($p < 0.001$)). Whereas T3 was significantly higher than T1 (23.65 to 21.65 ($p < 0.001$)). (Table 4) A significant change was found in cognitive function in T2 compared to T1 ($p < 0.001$) where 11 out of 16 subjects (68.8%) whose cognition changed from

normal to abnormal in T2. While a significant change in cognitive function also found in T3 compared to T1 ($p < 0.05$) where 7 out of 44 subjects (15.9%) whose cognition changed from abnormal to normal after HD. (Table 5) Executive function, attention, language and recall was lower in T2 compared to T1 ($p < 0.05$), Abstraction and orientation weren't different between T1 and T2 ($p > 0.05$). All cognitive domains improved in T3 ($p < 0.05$) compared to T1 and T2 except naming that didn't change over the session. (Table 6)

Table 3. Distribution of Cognitive Impairment

Test time	Cognitive Function	n	%
T1	Normal	16	26,7
	Abnormal	44	73,3
T2	Normal	5	8,3
	Abnormal	55	91,7
T3	Normal	23	38,3
	Abnormal	37	61,7

Table 4. Comparison of Total MoCA INA Score

Test Time	Mean	SD	P
T1	21,65	5,32	
T2	19,67	4,82	0,000
T3	23,65	5,38	0,000

Table 6. Comparison of Cognitive Function Domains

Cognitive Domains	Mean	SD	p
Executive (T1)	2,95	1,84	
Executive (T2)	2,52	1,74	0,000
Executive (T3)	3,20	1,85	0,001
Naming (T1)	2,63	0,71	
Naming (T2)	2,63	0,71	1,000
Naming (T3)	2,63	0,71	1,000
Attention (T1)	4,27	1,33	
Attention (T2)	3,57	1,18	0,000
Attention (T3)	4,68	1,31	0,000
Language (T1)	1,92	0,89	
Language (T2)	1,73	0,84	0,040
Language (T3)	2,20	0,73	0,000
Abstraction (T1)	1,15	0,73	
Abstraction (T2)	1,18	0,72	0,419
Abstraction (T3)	1,27	0,71	0,007
Recall (T1)	2,90	1,49	
Recall (T2)	2,17	1,51	0,000
Recall (T3)	3,55	1,62	0,000
Orientation (T1)	5,17	0,72	
Orientation (T2)	5,18	0,70	0,709
Orientation (T3)	5,45	0,70	0,000

Discussion

We evaluated the cognitive function in CKD stage 5 patients before, during and after a single HD session. The results revealed that on general assessment of cognition, the patients had low score of cognitive functions (MoCA INA < 26) in pre, intra and post HD. Our data suggest that HD patients with CI is common as seen

Table 5. Change in Cognitive Function during and after HD

T1		T2				T3			p
Normal				Total		Total			
Abnormal				Normal	Abnormal				
Total	Normal	N	5	11	16	16	0	16	0,016
		%	31,3%	68,8%	100,0%	100%	0.0%	100%	
	Abnormal	n	0	44	44	7	37	44	
		%	0,0%	100,0%	100,0%	15,9%	84,1%	100%	
		n	5	55	60	23	37	60	
	%	8,3%	91,7%	100,0%		61,7%	100%		

there were at least 44 patients (73,3%) who had CI at the start of HD (baseline). Consistent with Dasgupta et.al who reported 76% patients had at least mild CI at the start of HD session and 15% had severe CI.²⁰

In this study, we found a significant decline of cognitive function during HD in majority of patients as seen from MoCA INA score ($21,65 \pm 5,32$ to $19,67 \pm 4,82$, $p < 0.001$) and also 11 out of 16 patients (68.8%) whose cognition changed from normal to abnormal during HD ($p < 0.001$). A single HD session lead to cognitive improvement as seen from MoCA INA score ($21,65 \pm 5,32$ to $19,67 \pm 4,82$ to $23,65 \pm 5,38$, $p < 0.001$) and also 7 out of 44 patients (15.9%) whose cognition changed from abnormal to normal after HD ($p < 0.001$). This shows an acute fluctuating change in cognition over a single HD session and cognitive impairment can be exacerbated by the HD process itself.²¹ One prior study had addressed similar questions regarding the acute variation in cognitive function over a single HD session. Murray et al¹⁷ performed cognitive testing in 28 HD patients at four different time periods: 1 hr before, during (45–90 min from start), 1 hr after, and 24–30 hr after. Consistent to our finding that the cognitive function being worst during HD and best the day after.

The relationship between CI and HD is still not fully understood and the etiology is thought to be multifactorial.^{22,23} Hemodynamic stress during HD lead to temporary deterioration of cognitive function which subsequently improves several hours after HD as an effect of uremic toxin elimination.^{20,22,24} Hemodynamic stress during HD will be transmitted to and causes dysregulation of cerebral circulation.^{20,25} Fluid and electrolyte shift, intravascular volume loss during HD can also cause brain edema, decreased intracerebral pressure and perfusion to brain.^{9,26} And in the end, transient cerebral injury that occurs continuously will contribute to long-term CI in HD patients.²⁰

In this study, we found there were deterioration of multiple cognitive domains during HD including visuospatial, executive function, attention, language, and recall. After HD, we found an improvement of all cognitive domain except naming that didn't change over HD session. Consistent to our study, Murray et.al found deterioration in attention, memory and executive function during HD as well as Dasgupta et.al who found deterioration in attention, language, abstraction, and delayed recall.^{17,20}

This study have a significant clinical implications. Cognitive impairment during HD is associated with impaired capacity to actively process and retain information.²⁰ Providing information regarding health status, treatment plans, medication use, diet and other lifestyle changes is very important when patients have good attention, can remember the information communicated, plan and execute the steps needed to meet the goals of the treatment plan.^{11,27} Thus providing information to patients during HD may not be recommended especially after second half of the session because at that time it showed a significant deterioration in cognitive function.

Limitation

Our study has a number of limitations; firstly, MOCA-INA we used has good sensitivity in diagnosing cognitive disorders but cannot determine the degree of cognitive impairment. Secondly, the HD process itself may not be the only factor affecting the cognitive function in CKD patients. Further studies are needed to evaluate factors that affect the cognitive function in CKD.

Conclusion

There is an effect of single HD session on global cognitive function where executive function, attention, language, and recall were deteriorated during HD while abstraction and orientation didn't change. All Cognitive domains were recovered 24 hours after HD except naming that didn't change since the beginning

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APPENDIX

MONTREAL COGNITIVE ASSESMENT-Versi Indonesia (MoCA-Ina)

NAMA:
Pendidikan:
Jen. Kelamin:

Tgl Lahir:
Tgl Pemeriksaan:

VISUOSPASIAL/EKSEKUTIF

salin
gambar

Gambar jam (11 lebih 10 menit)
(3 poin)

POIN

[] [] []
bentuk angka jarum jam

.... /5

PENAMAAN

[]

[]

[]

.... /3

MEMORI

Baca kata berikut dan minta

subjek mengulangnya. lakukan 2 kali, meski berhasil
pada percobaan ke-1. lakukan recall setelah 5 menit

wajah

Sutera

Masjid

anggrek

merah

ke-1

ke-2

ATENSI

Baca daftar angka (1 angka/detik)

Subjek harus mengulangi dari awal [] 2 1 8 5 4

Subjek harus mengulangi dari belakang [] 7 4 2

.... /2

Baca daftar huruf. subjek harus mengetuk dengan tangannya setiap kali huruf A muncul. poin nol jika ≥ 2 kesalahan

[] FBACMNAAJKLBAFAKDEAAAJAMOF AAB

.... /1

Pengurangan berurutan dengan angka 7. Mulai dari 100 [] 93 [] 86 [] 79 [] 72 [] 65

4,5 hasil benar: 3 poin, 2 atau 3 benar: 2 poin; 1 benar: 1 poin, 0 benar: 0 poin

.... /3

BAHASA

Ulangi: Wati membantu saya menyapu lantai hari ini. []

Tikus bersembunyi di bawah dipan ketika kucing datang. []

.... /2

Sebutkan sebanyak mungkin kata yang dimulai dengan huruf F [] (N ≥ 11 kata)

.... /1

ABSTRAKSI

Kemiripan antara, contoh pisang - jeruk = buah [] kereta - sepeda [] jam tangan - penggaris

.... /2

DELAYED RECALL

Harus mengingat kata

TANPA PETUNJUK

wajah

Sutera

Masjid

anggrek

merah

[]

[]

[]

[]

[]

poin untuk recall
tanpa petunjuk

Opsional

petunjuk kategori

petunjuk pilihan ganda

.... /5

ORIENTASI

[] Tanggal

[] Bulan

[] Tahun

[] Hari

[] Tempat

[] Kota

.... /6

Normal $\geq 26 / 30$

Total

.... /30

Dilakukan oleh.....

Tambahkan 1 poin jika pend. ≤ 12 tahun