The Cerebrovascular and Neurocognitive Effects of Haemodialysis

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Background

- Cognitive impairment (CI) is common in those with CKD; it is estimated that for each 10ml/min loss in GFR there is an associated 11% increase in prevalence of CI
- Reports suggest that up to 70% of those on haemodialysis (HD) for established renal failure (ERF) have moderate to severe CI
- In addition to the effect on patient concordance with treatment CI is an independent risk factor for mortality - yet remains poorly recognised
- Analogous to myocardial stunning noted during dialysis, cerebral stunning is likely and may predispose to progressive cognitive decline.
- We performed assessments of cognition and cerebral blood flow during and out with dialysis to assess the impact of HD on cerebral blood flow and function

Aims

- Describe the frequency and association of CI in patients on HD for ERF
- Describe alterations in cerebral blood flow during the HD session
- Assess for correlation between alteration in cognitive function and intradialytic cerebral blood flow

Method

- Prospective observational study in adult patients on HD for ERF
- We excluded those with documented diagnoses of cerebrovascular disease (clinical or on previous imaging) or cognitive impairment
- A neurocognitive assessment was performed during and out-with dialysis– separated by a 3-4 week gap to abate potential learning effects
- Assessment consisted of a basic screening tool for cognitive impairment, the Montreal Cognitive Assessment (MOCA), and further assessments chosen to assess multiple domains. Namely - language (Semantic memory and Phonemic fluency), processing speed (Letter Digit Substitution Test (LDST)), executive function (Trail Making Test A (TMT-A) & Trail Making Test B (TMT-B)) and memory (Hopkin's Verbal Learning Test (HVLT))

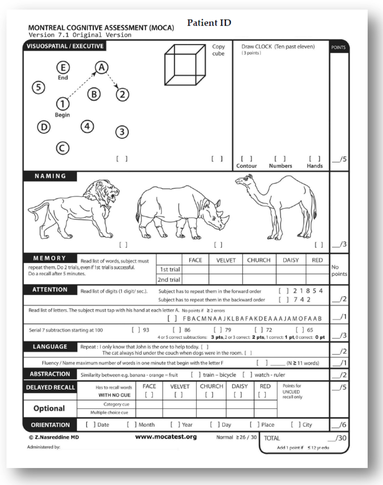

Figure 1 *Examples of Cognitive Assessments - MOCA and TMT-B*

- Real-time mean flow velocity (mfv) was recorded at the middle cerebral artery (MCA) using transcranial doppler before, during & after HD, Fig. 2
- Cognitive impairment was defined using established MOCA cut-offs and changes in multiple domains of cognitive function correlated with alterations in mfv using Spearman's Rank correlation
- Data were analysed using SPSS v22

Results

- 88 patients completed both visits, median age 59 years [IQR 51,67]
- 45.5% were female and the median duration on renal replacement therapy (RRT) was 1.76 years [IQR 0.6,4.0]. Further demographics are shown in table 1
- Using the accepted MOCA score cut off of <26 to define frequency of cognitive impairment, 50% of this cohort had objective evidence of CI
- Aside from presence of hypertension (95.5 v 81.8%, *p=0.04)*, and higher pre-dialysis systolic BP in those with cognitive impairment (143.0 v 132.4mmHg, *p=0.01*), there were no significant differences in demographics between groups
- Participants scored lower on tests of processing speed and executive function during dialysis, table 2
- A significant decline in mfv was noted following dialysis, 49.8 to 43.2cm/s, P<0.001, figure 3. The decline correlated with UF volume (r=0.49, *p<0.001*) and diabetes (r=-0.29, *p<0.01*)
- Decline in scores for language & executive function significantly correlated with a dialysis-related fall in mfv, table 2

	n=88
Median Age, years [IQR]	59 [51,67]
Female (%)	40 (45.5)
Ethnicity (%)	
White British	92 (96.9)
South Asian	4 (4.1)
Other	1 (1.0)
Primary Renal Diagnosis (%)	
Glomerulonephritis	20 (20.6)
Interstitial	20 (20.6)
Multisystem	20 (20.6)
Diabetes	18 (18.6)
Other	19 (19.6)
Access (%)	
AV access	69 (71.1)
TCVC	28 (28.9)
Past Medical History (%)	
Hypertension	85 (87.6)
Diabetes	32 (33)
Depression	21 (21.6)
Median duration of RRT, y [IQR]	1.76 [3.4]
Mean SBP [SD]	143 [37.2]
Mean DBP [SD]	72.7 [15.4]
Mean UF [SD]	2.1 [1.1]
Mean URR [SD]	73 [8]
Year of education (%)	
8-12	61 (62.9)
13-21	36 (37.1)
Cognitive Impairment (%)	
Normal (MOCA ≥26)	44 (50)
Mild-Moderate (<26)	44 (50)

Table 1 *Cohort Demographics*

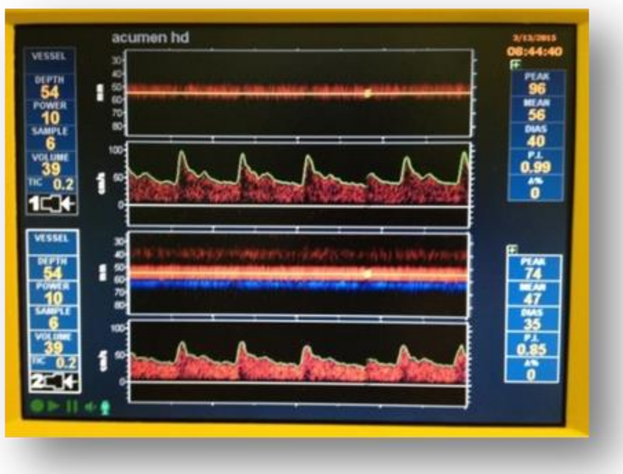

Figure 2 *Screen shot of transcranial doppler unit demonstrating bilateral insonation of middle cerebral arteries*

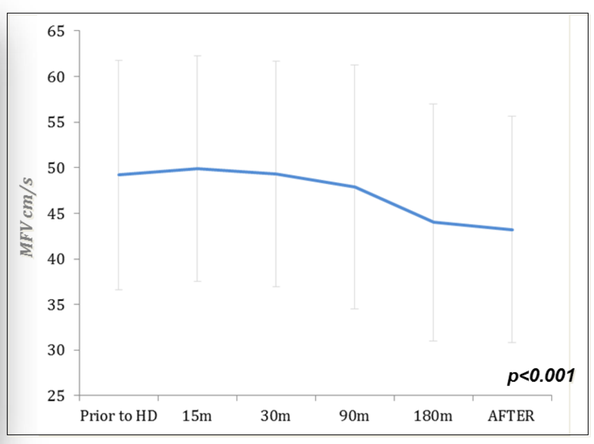

Figure 3 *Alteration of mfv of MCA before, during and after dialysis. A significant derease in mfv persists following HD, p<0.001*

Assessment	Day-Off Score Median [IQR]	Intradialytic Score Median [IQR]	*p*	Spearman's Rank Δ Scores - %Δmfv	*p*
MOCA	25 [21,26.5]	24 [22,26]	0.72	-0.22	0.06
Semantic Memory	18 [15,22]	18 [15,21]	0.27	-0.20	0.10
Phonemic Fluency	34 [25,43.5]	33 [26,39]	0.48	-0.27	**0.02**
LDST	25 [20,30]	21 [17,26]	**<0.001**	0.20	0.09
TMT-A *(time, secs)*	35.5 [26.9,50]	38 [27,51]	0.63	0.44	**<0.001**
TMT-B *(time, secs)*	75 [54,112]	89.5 [62,141]	**<0.001**	0.37	**0.004**
HVLT Recall	20 [17,23]	22 [19,25]	**<0.001**	-0.15	0.22
HVLT Delay	6 [4,9]	7 [5,9]	0.13	-0.11	0.38
HVLT Retention	78.9 [60,100]	80 [62.5,90]	0.90	0.08	0.48
HVLT Discrimination	10 [9,11]	10 [9,11]	0.80	-0.02	0.90

Table 2 *Median scores on dialysis and on day-off [Wilcoxon Signed Rank Test], and Spearman's Rank correlation of different in scores against percentage change in mean flow velocity . Correlations relate to change in mean flow velocity and difference in score (day-off score minus intradialytic score)*

Discussion

- Occult cognitive impairment is common and demonstrably worse during dialysis
- Cerebral blood flow is lowered by HD and related to UF volume and degree of cognitive function seen
- Further study examining the transient effects of changes in mfv and cognitive function on longer term cognitive decline are ongoing

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