A SINGLE-BLIND RANDOMISED CONTROLLED CROSSOVER STUDY OF RECOVERY TIME IN HIGH-FLUX HAEMODIALYSIS AND HAEMODIAFILTRATION

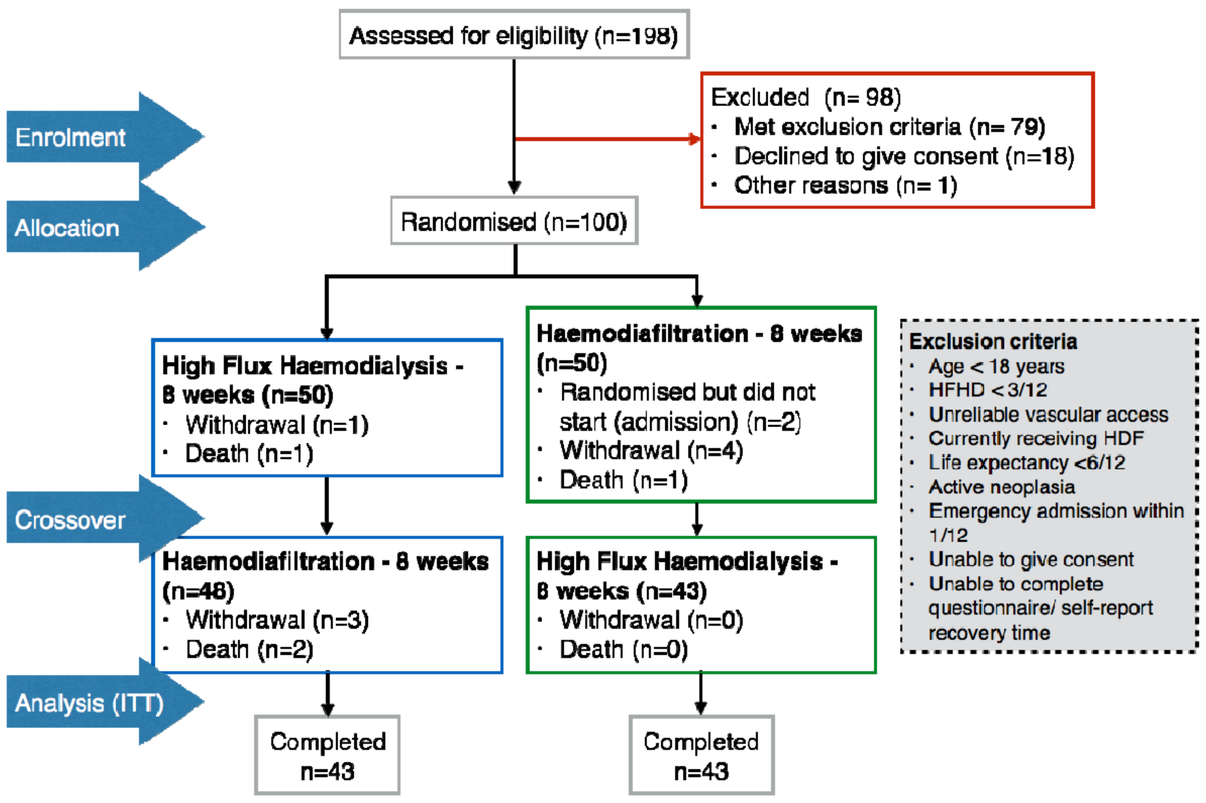
JR Smith*, N Zimmer*, E Bell*, B Francq, A McConnachie**, R Mactier***

Glasgow Renal and Transplant Unit* and Robertson Centre for Biostatistics, University of Glasgow**

Introduction and Aims

High-flux haemodialysis (HFHD) and **haemodiafiltration (HDF)** are widely used to treat patients with end-stage renal disease. RCTs comparing HFHD with HDF show mixed results, however high-efficiency online HDF (convective volumes > 23L) was associated with reduced morbidity and mortality in a recent RCT (1). In the DOPPS, post-dialysis recovery time predicts patient survival (2). We aimed to compare self-reported post-treatment recovery time in HFHD and HDF.

Figure 1 – CONSORT diagram and exclusion criteria



Methods

Patient-blinded, randomised controlled crossover design (see Figure 1) in which each patient was randomised to receive eight weeks of HFHD, followed immediately by eight weeks of HDF, or vice versa (ClinicalTrials.gov Identifier: NCT01862679). Patients were recruited from two satellite dialysis units. The study ran for 9-months between July 2013 and March 2014.

The primary outcome was post-treatment recovery time. Secondary outcomes; Health Related Quality of Life (HRQoL) using KDQOL-SF™, symptomatic hypotension, thrombosis of the extracorporeal circuit and patients' preferred treatment modality.

In order to detect a 20% absolute reduction in recovery time with 90% power, we calculated that 82 patients would need to complete the study (41 in each group). Mixed models (for the cross-over design) and paired-t tests (to simplify the model) were carried out in order to assess and compare the treatment effects. Categorical variables were assessed across the treatments by Odds ratios and Fisher exact tests.

Table 2 – Baseline Characteristics

Characteristic	HFHD then HDF	HDF then HFHD	p value
Female	40	38	1
Age (years)	64.5 (14.8)	65.9 (13)	0.629
Dialysis vintage* (months)	79.6 (104.1)	39.9 (39.1)	0.222
Access			
Fistula	62	74	
Graft	0	2	0.194
Line	38	24	
SBP (mmHg)	144 (22)	142 (18)	0.691
DPB (mmHg)	67 (12)	70 (11)	0.273
Post HD weight* (kg)	79.3 (21.1)	74.2 (17.8)	0.231
UF volume (ml)	1995 (681)	1644 (668)	**0.011**
PRD			
Glomerular	26	26	1
Tubulointerstitial	10	12	1
Systemic	34	26	0.513
Hereditary	6	14	0.318
Miscellaneous	24	22	1
Transplant listed	26	16	0.326
Smoking			
Current	22	32	
Ex-smoker	34	26	0.511
Never smoked	44	42	
Diabetes	30	22	0.495
Ischaemic Heart Disease	40	34	0.679
Peripheral Vascular Disease	28	10	**0.04**
Stroke	20	14	0.595
Neoplasia	12	2	0.112
Charlson Comorbidity Score#	6.7 (2.4)	6.2 (2.1)	0.368

Data presented as % or Mean (SD). *log transformed prior to t-test. #non-parametric test.

Results

There was no difference in self-reported post-treatment recovery time between HFHD and HDF (HFHD 197 minutes (sd 400), HDF 222 minutes (sd 422), p=0.266)– see Figure 2.

Parity remained when crossover analysis and session effects were taken into account. Additionally, no difference was observed in either physical (HFHD 33, HDF 33, p=0.959) or mental health (HFHD 81, HDF 78, p=0.638) composite HRQoL scores.

Figure 2 – Crossover analysis of recovery times (log transformed)

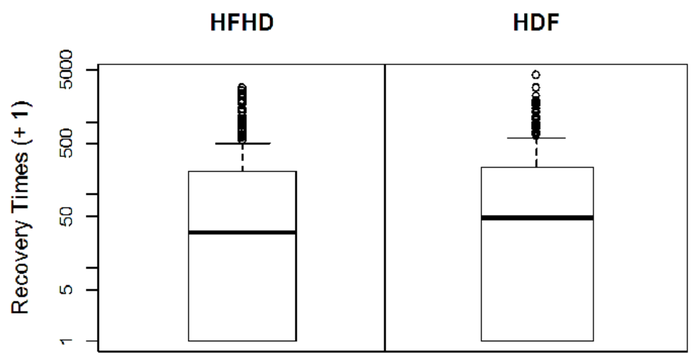


Table 3 confirms that variables such as treatment time, blood flow and ultrafiltration volume remained constant. The mean achieved convection volume during HDF was 20.8L.

Table 3 – Treatment variables by treatment modality

	HFHD Mean (SD)	HDF Mean (SD)	Paired t-test	Cross-over
Treatment Time (mins)	250 (17)	250 (17)	p=0.106	p=0.121
Blood Flow (mls)	315 (27)	313 (28)	p=0.712	p=0.63
Ultrafiltration Vol (mls)	1749 (718)	1723 (672)	p=0.351	p=0.429
Pre Rx SBP (mmHg)	145 (21)	143 (21)	**p=0.024**	**p=0.029**
Pre Rx DBP (mmHg)	69 (12)	69 (12)	p=0.141	p=0.147
Post Rx SBP (mmHg)	126 (20)	125 (18)	p=0.066	p=0.078
Post Rx DBP (mmHg)	64 (10)	63 (10)	p=0.118	p=0.119

HDF was associated with an increase in episodes of symptomatic hypotension and risk of thrombosis compared with HFHD (Table 4).

Table 4 – Adverse events recorded during treatment sessions

	HFHD	HDF	OR (95% CI)	p value
Symptomatic hypotension	5.2%	8%	1.57 (1.22, 2.03)	**<0.001**
Increase in tinzaparin dose or clotting of circuit	0.7%	1.8%	2.71 (1.43, 5.45)	**0.001**

Haematological and biochemical parameters were measured at the middle and end of each 8-week treatment period. The majority of these variables were equivalent. However there were small but statistically significant differences in serum albumin (HFHD 33 g/l, HDF 32 g/l, **p<0.001**) and chloride (HFHD 100 mmol/l, HDF 101 mmol/l, **p=0.015**).

Blinding was maintained in all but 2 patients. Those who remained blinded were asked for treatment modality preference; 52 had no preference, 21 preferred HDF and 11 preferred HFHD. 8 patients felt able to guess treatment order based on their symptoms, 5 were correct and 3 incorrect.

Conclusions

In this prospective patient-blinded randomised controlled crossover trial we found that there was no difference in the primary outcome of self-reported post-treatment recovery time between HFHD and HDF. This result is supported by our findings that HRQoL was also equivalent between treatments. While the small increase in clotting events is in keeping with previous findings, the increased incidence of hypotensive events during HDF, and associated small reduction in pre-treatment blood pressure was not anticipated based on previous data.

Where debate regarding the medical case for HDF over HFHD persists and patient preference is of increasing importance in clinical practice, these data further inform the discussion around choice of extracorporeal treatments.

References

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2) Rayner, H.C., *et al*. *Am J Kidney Dis* **64**, 86-94 (2014)

Contact

Dr James R Smith

jsmith82@nhs.net

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James Smith

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